Networks and the Development of the Irish Biotechnology Sector

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Abstract

Biotechnology, an umbrella term describing combinations of engineering and scientific knowledge from an array of disciplines used to produce products and processes from living organisms, has been identified as a key sector for future economic developments among industrialised and industrialising nations as it blurs traditional boundaries between various industries. The Irish Government has introduced a series of initiatives to facilitate the development of an internationally competitive indigenous biotechnology sector since the late 1990s, yet no in-depth analysis of the sector relative to international sectoral characteristics, structures, or policy themes have informed their design or implementation. This thesis analyses the Irish sector in the context of global sectoral developments by studying the Post-Fordist organisational structure of the international sector, where biotechnology firms interact with various actors at different stages of the sectoral value chain in a variety of innovative networks determined by place specific actor and institution endowments that form local knowledge communities. Through qualitatively investigating the Irish sector's actors and collaborative network structure, the thesis analyses the implications of the nature and character of these elements for the sector's future sustainability and development, and appraises existing Government policies relating to sectoral developments. The thesis found that the on-going initiatives have facilitated significant advances, yet have not addressed the legacy of pre-initiative resource and skill capacity weaknesses, while the sectoral value chain is fragmented as actors have developed poor networking arrangements due to their conservative natures, and the relative absence of key sector actors, skills and resources. These issues demonstrate that a complex overarching policy framework is required so as to engender the long-term development of a regionally tailored, systems-based support ecosystem which addresses existing structural weaknesses, and which facilitates and drives entrepreneurial and innovative activities throughout the sector's value chain.

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List of Acronyms

- ACSTI: The Advisory Council for Science, Technology and Innovation
- AUA: The Atlantic University Alliance
- CSETs: The Centres for Science, Engineering & Technology
- DES: The Department of Education and Skills
- DETI: The Department of Enterprise, Trade and Innovation
- DMMC: The Dublin Molecular Medicine Centre
- DNA: Deoxyribonucleic Acid
- EEC: The European Economic Community
- EI: Enterprise Ireland
- EIFR: Entrepreneurial and Innovative Functional Resource
- EIBD: Enterprise Ireland's Biotechnology Directorate
- EPA: The Environmental Protection Agency
- EU: The European Union
- FDI: Foreign Direct Investment
- FPs: Framework Programmes
- GATT: The General Agreement on Tariffs and Trade
- GDA: The Greater Dublin Area
- GDP: Gross Domestic Product
- GMOs: Genetically Modified Organisms
- HEA: The Higher Education Authority
- HRB: The Health Research Board
- HSE: The Heath Service Executive
- IBEC: The Irish Businesses and Employers Confederation
- IBIA: The Irish BioIndustry Association
- ICSTI: The Irish Council for Science, Technology and Innovation
- IFSC: The International Financial Services Centre
- ILOs: Industrial Liaison Offices
- IP: Intellectual Property
- IPO: Initial Public Offering
- IoTs: Institutes of Technology
- JIT: Just in Time delivery
- NAMA: The National Asset Management Agency
- NBP: The National Biotechnology Programme
- NBST: The National Board for Science and Technology
- NCP: Network Cooperation Programme
- NDP: The National Development Plan
- NESC: The National Economic and Social Council
- NICTs: New Information and Communication Technologies
- NIH: National Institutes of Health
- NSS: The National Spatial Strategy
- NTMA: The National Treasury Management Agency
- NUIM: National University of Ireland, Maynooth
- OECD: The Organisation for Economic Co-operation and Development
- PBCs: Proto Biotechnology Clusters
- PC: Proto Cluster
- PCR: Polymerase Chain Reaction
- PCT: A Patent Co-operation Treaty
- PREOs: Public Research and Education Organisation
- PRTLI: The Programme for Research in Third Level Institutions
- rDNA: Recombinant Deoxyribonucleic Acid
- R&D: Research and Development
- RHs: Research Hospitals
- RIs: Research Institutes
- RTCs: The Regional Technical Colleges
- RTDI: The Research, Technological Development and Innovation fund
- SFI: Science Foundation Ireland
- SME: Small and Medium Enterprise
- STI: Science, Technology and Innovation
- STIAC: The Science, Technology and Innovation Advisory Council
- SV: Silicon Valley
- SWOT: Strengths, Weaknesses, Opportunities and Threats analysis
- TFF: The Technology Foresight Fund
- TNC: Transnational Corporations
- TTOs: Technology Transfer Office
- UK: The United Kingdom
- UL: The University of Limerick
- VCs: Venture Capitalists

CHAPTER 1:
INTRODUCTION

1.1 SETTING THE SCENE

Biotechnology is an umbrella term used to describe a combination of engineering and scientific knowledge and techniques derived from advances across a large array of disciplines and sub-technologies (including cellular and molecular biology, chemistry, physics, and information science) to produce new or improved products, processes and services from living organisms (Downey, 1979; Kenney 1986; Panetta, 2006).

Due to its wide scientific base, biotechnology impacts on a variety of established industries, particularly through facilitating innovative developments across industries by blurring traditional boundaries which exist between them. As such, biotechnology has been identified as one of the key sectors for future economic developments among industrialised and industrialising nations (Massachusetts Biotechnology Council, 2002; European Commission, 2012).

This chapter is divided into three sections. The remainder of the following section places the thesis into its proper context in relation to the development of biotechnology, and the development of the international biotechnology sector. The second section details the specific focus of the thesis. The structure of the thesis is presented in the final section.

1.1.1 The development of biotechnology

Biotechnology is based on a series of laboratory-based scientific advances which have occurred since the second half of the 20th century. The foundation of modern biotechnology can be traced to 1940, when Oswald Avery (of the Rockefeller Institute, New York) demonstrated that deoxyribonucleic acid (DNA) was the transferring factor in genetic information, and was the fundamental component of genetic material (Evers, 2002; Biotechnology Industry Organization, 2001; Europa, 2006; Wallman, 1997).

The second, but more important breakthrough, occurred in 1953 when Francis Crick and James Watson (of Cambridge University) and Rosalind Franklin (of King's College, London) discovered the genetic code by which the DNA double helix (Figure 1.1), the basic structure of life, governs the reproduction of cells in all living organisms (Access Excellence, 2002a; Time.com, 2000).

This discovery subsequently initiated the microbiology revolution, and was followed by further breakthroughs which played central roles in the subsequent development of the modern biotechnology industry, in particular:

- the development of recombinant DNA (rDNA) technologies in 1973, by Stanley Cohen (of Stanford University) and Herbert Boyer (of the University of California, San Francisco). This development facilitated genetic engineering, i.e. scientists could now alter the genetic coding of DNA to give micro-organisms specific qualities not ordinarily found in nature, and;
- the development of the Polymerase Chain Reaction (PCR) technique in 1983 by a team of scientists led by Kary B. Mullis (of the Cetus Corporation, Berkley, California). PCR deciphers the genetic material of organisms and analyses the functions of genes, facilitating the analysis of the genetic causes behind infections, cancers and genetic disorders (Chiron Corporation, 2002; Kayvon et al., 2002b; Feldman and Francis, 2003).

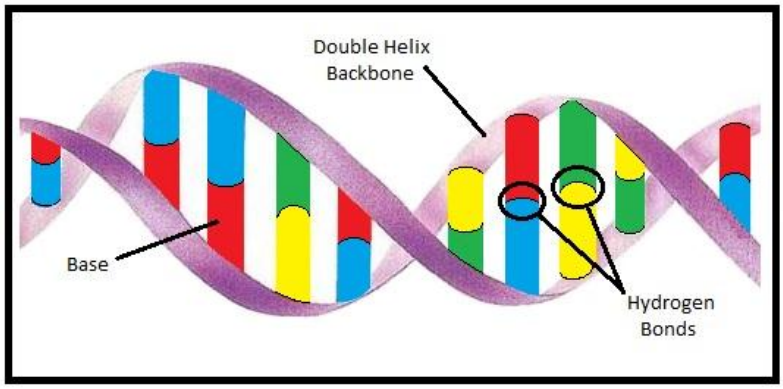


Figure 1.1.: Structure of the Deoxyribose Nucleic Acid (DNA) double helix (After Watson and Crick, 1953).

1.1.2 The development of the biotechnology industry

The origins of the modern biotechnology industry can be traced to the San Francisco Bay Area in 1975. Robert Swanson, a Silicon Valley-based venture capitalist who had a background in chemistry, had come to the conclusion that the many laboratory-based microbiological research projects conducted in US universities/research centres had latent commercial promise. Swanson interviewed researchers to determine whether such research could be commercialised in a viable manner. A casual meeting with Herbert Boyer, the co-developer of rDNA in 1973, confirmed Swanson's suspicions about the commercial potential of biotechnology research (Access Excellence, 2002b, 2002e; The Bancroft Library, 2002; Zhang and Patel, 2005; Delerue and Lejeune, 2011).

Swanson and Boyer subsequently established Genentech, the world's first 'new' biotechnology firm (bio-firm), in 1976 to create a synthesis of human insulin. Genentech successfully licensed its human insulin technology to pharmaceutical Transnational Corporation (TNC) Eli Lilly in 1978, and became the first bio-firm to float on the US stock market in 1980, raising a record breaking $35 million with its initial public offering. Due to its sustained success, Genentech attracted strong interest from TNCs, culminating in Swiss-based Hoffman La Roche purchasing a majority stake in 1990, followed by an outright purchase in 1999 (Roche, 2000, 2002; Genentech, 2002a; 2002b).

The manner of Genentech's formation and rapid development created a bio-firm development 'template' for the international biotechnology sector (bio-sector). This can be summarised as follows; academic researchers commercialise their research by establishing a bio-firm through venture capital (VC) support, the bio-firm's business activities are optimised through the advice and guidance of the VC firm, and subsequently the bio-firm is floated on the stock market and/or strategic alliances with a TNC are sought so as to access the necessary knowledge sets and revenues required in developing products or processes, and to continue generating high quality research (Krafft et al., 2011).

In the wake of Genentech's establishment, the international bio-sector quickly developed through major governmental support and funding, as the potential range and impact of biotechnology-derived applications were recognised as being a major engine for economic growth. The various technologies used in biotechnology have subsequently been introduced in most developed and underdeveloped regions as the 'raw materials' needed to successfully develop a bio-sector, i.e. high quality scientific research and sums of intelligently-invested money, are not the sole province of a single country or region (Abate, 2001).

It must be noted that bio-sectors, internationally, have been fashioned after various development patterns evident in the US bio-sector, while they have also idiosyncratic versions of US institutions and organisational structures (Biotechnology Industry Organization, 2002: 2007).

The global spread of biotechnology has also been driven by the significant support and

funding of TNCs. While there have been consistent problems in turning scientific biotechnology advances into marketable products for a variety of reasons, including ethical and political issues, one clear exception is that of biotechnology-derived pharmaceutical products. Due to their enormous commercial value, research on new pharmaceutical drugs, therapies and diagnostics has grown rapidly due to massive investments from pharmaceutical TNCs. TNCs have increasingly focused on biotechnology as it complements their core activities, while also replacing the traditional chemical knowledge base upon which pharmaceutical products were previously developed (this issue is detailed further in chapter 2) (Irish Council for Science Technology & Innovation, 2005).

There are presently two 'main' foci in the biopharmaceutical sector:

- diagnostic products, i.e. procedures, devices and chemicals that screen, detect, diagnose and monitor diseases, which are relatively quick to develop for the market place, and;
- biotechnology-derived pharmaceutical drugs, i.e. pharmaceutical drugs developed through genetic engineering, which are targeted towards specific diseases or conditions (Panetta, 2006; Dodgson et al., 2008).

Biotechnology's importance for the global pharmaceutical industry continues to deepen as the science and its possible industrial applications expand into new areas. This expansion has been driven by the completion of the human genome project in 2001. This project has the potential to revolutionise all aspects of the biotechnology industry, and expand its reach and impact into areas previously unimagined. Indeed, most of the technological advances in pharmaceuticals over the last ten years have developed from genomic research:

> "...genomics has caught the attention of the traditional pharmaceutical industry to a greater extent than any other early-stage technology in the biotechnology industry's history. Companies are vying to stake out patent-protected territory in what they believe will be the therapeutic battlefield of the 21st Century: the human genome." (Author unknown, quoted in ETC Group, 1994).

Genomic research represents the next phase of biotechnological development by further blurring the boundaries between the pharmaceutical, agricultural, chemical, environmental, energy and computer industries (Donnelly and Smyth, 2001; Human Genome Project Information, 2002b, 2002c).

1.1.3 The unique structure of the international biotechnology industry

The modern bio-sector is a structurally-complex post-Fordist industry. Post-Fordism emerged in the late 1960s/early 1970s, superseding the previous dominant industrial structure of the 20th century, the vertically-integrated, mass assembly production line-based Fordist model of industrial organisation (these organisational forms are detailed further in chapter 2) (Dicken, 1998).

Post-Fordist firms are characterised as being small, flexible, and highly adaptable/sensitive to market changes and demands. Their development was facilitated by the impact of globalisation and advances in new information and communication technologies (NICTs) which allowed production structures to fragment as individual firms focused on specific niche markets through specialising in specific areas of expertise. The resultant fragmentation of markets and production processes has led to the economies of industrialised countries moving away from traditional forms of industrial manufacturing towards service- and knowledge-intensive economic sectors, such as biotechnology (Capello, 1996; Dicken, 1998).

Additionally, Post-Fordism, globalisation (e.g. borderless markets), and the hypermobility of finance have emphasised regional economic distinctions in relation to place specific concentrations of specialised skills, knowledge, institutions, and businesses. Such agglomerations allow firms to benefit from both market and non-market externalities/spillovers, which increase local endogenous innovation and productivity. In effect, "regional economies, not national economies, are now the salient foci of wealth creation and world trade" (Martin and Sunley, 2001: 3).

The biotechnology industry's complex Post-Fordist value chain can be characterised as being formed around different inter-actor relationships found between third level-based researchers who seek to commercialise research through establishing a bio-firm and forming alliances with VCs and/or TNCs, i.e. the 'template' created by Genentech, as detailed above (these different actors and relationships are detailed further in chapter 3). Such developments are supported by Government agencies through the creation of a positive and supportive policy environment, and other sectoral support actors, such as specialist supply and service firms.

As the international bio-sector has evolved, the inter-actor networked structure of the

bio-sector and its value chain, have grown in complexity, leading to the international bio-sector being labelled the training ground of corporations in the 21st century (Boje, 2001; Harrison, 1997).

However, networks are not solely at the heart of the development of bio-sectors, as they form and emerge from distinct geographic roots; "...geography played a key role in the industry's evolution and remains an important feature even today" (Owen-Smith and Powell, 2007: 63). Many of the actors and organisations that forged, and continue to support the complex relationships found in the international bio-sector are located in close geographic proximity to each other, meaning these networks are spatially concentrated in what are identified as industrial clusters (detailed further in chapter 2) (Visser and Boschma, 2002; Romanelli and Feldman, 2007).

The industrial organisation of such a complex structured sector poses significant issues for policy makers, as the various roles and demands of different actors, networks, and clusters in the development of a bio-sector require multi-faceted and inter-related policy approaches. Many Governments wishing to develop indigenous bio-sectors have struggled to develop and maintain adequate policy coverage due to the rapid advances and developments of bio-sectors at local and global levels. This is reflected in the very limited number of hub bio-sectors that have emerged internationally, as detailed further in chapter 3 (Wolfe, 2005; Feldman and Braunerhjelm, 2007).

1.2 FOCUS OF THE THESIS

The Irish Government first identified biotechnology as a key sector for Ireland's future economic development in the late 1970s. However, concerted efforts to facilitate the development of an internationally competitive indigenous bio-sector have only occurred since the late 1990s through a series of investment programmes which have mainly focused on addressing decades of underinvestment and underdevelopment in many areas of the sector's value chain, in particular through addressing infrastructural- and skills-related issues in the country's third-level institutions (this is detailed further in chapters 5 and 6). These issues have impacted on the development of the characteristically complex, network dependent sectoral value chain (as detailed above) within the Irish bio-sector (this is detailed further in chapters 7 and 8) (Burke et al., 2003; Cogan and McDevitt, 2000).

This thesis *qualitatively* investigates the structure of the Irish bio-sector, in comparison to the structures found in the international bio-sector's key hubs, to determine the strengths and weaknesses of the inter-actor networking arrangements which have developed among the bio-sector's actors, and how they are impacting on the development of the indigenous bio-sector. This research has an important theoretical dimension in seeking to locate the networking configuration of the Irish bio-sector in the context of general global developments. It also seeks to develop policy proposals to indigenously replicate the complex structures and supports, such as inter-actor networks and industrial clusters, which have underpinned the successful development of the international industry's key bio-sectors.

The overall aim of this thesis is to explore:

- the configurations of the collaborative network structures among the Irish bio-sector's actors, and;
- the implications of these structures for the future sustainability and development of the indigenous bio-sector.

In particular the thesis:

1. identifies sectoral actors in the Irish biotechnology sector,
2. examines inter-actor networks and interactions, and reflects on their uniqueness to Ireland;
3. appraises the functions, performances, and weaknesses of inter-actor sectoral networks and clusters in Ireland in comparison to their international counterparts, and;
4. appraises existing Irish Government policies relating to the indigenous bio-sector.

1.3 STRUCTURE OF THE THESIS

The dissertation is divided into ten chapters.

Chapter 2 details how Post-Fordist firms superseded Fordist industrial structures through their ability to rapidly respond to market changes due to their fragmented, though integrated production process which are coordinated through inter-actor networks. This chapter details what inter-actors networks are, their key features, what motivates actors to form networks, the role of inter-actor networks in facilitating

innovative developments, as well as how their form and behaviour are determined by the spatial contexts and social relationships in which they develop. This chapter then details the theory of industrial clusters, i.e. more advanced forms of industrial organisation which are inherently organised/based on inter-actor networks. Finally, the chapter discusses Government policy measures which seek to facilitate new cluster developments, and to optimise the development of existing clusters, derived from international case studies. This chapter, ultimately, lays the theoretical foundation from which the remainder of the thesis is constructed.

Chapter 3 applies the theoretical descriptions of Post-Fordist institutional and geographic organisation, i.e. inter-actor networks and industrial clustering (as detailed in chapter 2), to the international bio-sector to create the theoretical foundation upon which the subsequent analytical chapters are based. The chapter presents a typology of the main sectoral actors found in the international bio-sector, which is derived from observations of key bio-sectors, and a template of the key formal and informal inter-actor networks found throughout the biotechnology innovation process, using the previously detailed actor typologies. The chapter discusses the international bio-sector's tendency towards industrial clustering, and then presents an analysis of cluster policy measures that seek to engender and support new and existing biotechnology cluster development.

Chapter 4 outlines the methodological approach used to conduct the empirical research on the Irish bio-sector and its network structure, based upon the sectoral actor and network typologies presented in Chapter 3. This methodology informs the remainder of the thesis.

Chapter 5 places the remaining analytical chapters into their proper context by presenting a general review of Ireland’s economic development since the early 1920s, and discusses the evolution, and interconnectedness, of policies relating to the indigenous bio-sector, including the government's industrial, Science, Technology and Innovation policies, as well as the evolution of policy thinking in relation to networks and clusters.

Chapter 6 applies the actor typologies detailed in chapter 3 to the Irish bio-sector to provide a comparative overview of the indigenous bio-sector’s key actors. This

overview is derived from the sectoral review, survey, and actor interviews detailed in chapter 4.

Chapter 7 applies the inter-actor network typologies found in the international bio-sector, as presented in chapter 3, to the Irish bio-sector, using the actor typologies presented in chapter 6. The chapter also analyses the development and evolving nature of the bio-sector's network arrangements, and their regional characteristics.

Chapter 8 presents a comprehensive range of systems-based policy areas that address the existing issues that undermine the indigenous bio-sector's development, so as to facilitate the development of an advanced, highly entrepreneurial and innovative bio-sector. These policy suggestions are derived from an analysis of structural strengths that are evident in the indigenous bio-sector, upon which on-going efforts to develop the bio-sector can build, as well various obstacles that exist in the bio-sector's value chain which will undermine and impinge on future sectoral development efforts. This analysis emerges from and builds upon the findings of chapters 5, 6 and 7, while the policies are derived using the bio-system policy template developed in chapter 3.

Chapter 9 presents a comparative analysis between Ireland and the international hub and non-hub bio-sectors. This analysis focuses on the core areas of this study, so as to place the findings of the previous analysis chapters into their proper contexts, and to identify the contributions of the Irish bio-sector's analysis to advancing our understanding of the international bio-sector.

Chapter 10 concludes the thesis, presents the main argument of the thesis, and its findings. Additionally, the research project's contribution to current research is also discussed.

CHAPTER 2:
THE STRUCTURES AND DEVELOPMENT OF POST-FORDIST INDUSTRIAL NETWORKS AND CLUSTERS

2.1 INTRODUCTION

This chapter details advanced forms of industrial organisation which are increasingly important for regional economic development and technology intensive industrial sectors, i.e. inter-actor networks and industrial clusters. The chapter details how Post-Fordism has changed the economic geographic distribution of production through superseding Fordist industrial structures. These structures are characterised by the spatial fragmentation of production processes, through advanced and spatially integrated production processes that are coordinated through different forms of inter-actor networks. Networks are crucial elements in facilitating innovative developments in knowledge intensive high-tech sectors, their form and behaviour are determined by the spatial contexts and social relationships in which they develop. Where spatial agglomeration of actors and networks occur, industrial clusters may develop. Clusters are highly advanced and localised industrial systems that are inherently organised/based on networks, and contribute to the innovation and competitiveness of their constituent actors. Clusters are defining characteristics of modern high-tech industrial sectors.

This chapter is divided into four sections. The first section traces the emergence and development of the Post-Fordist production system since the late 1960s/early 1970s, and the development of inter-actor networks. The second section presents a theoretical analysis of the structures and functions of inter-actor networks, how collaborative networks facilitate innovative activities, and how geography and social relationships impact on their formation, structures and functions. The third section discusses how networks develop into 'networks of networks' i.e. industrial clusters. This section details Porter's (1998) cluster model, and presents the four determinants of competitive advantage which determine the context in which clusters emerge. This section also discusses the complexities of promoting industrial clusters through policy actions, in relation to efforts seeking to facilitate a cluster's emergence, and also in relation to optimising an existing cluster's development trajectory. The conclusions are presented in the final section.

2.2 FROM FORDIST TO POST-FORDIST PRODUCTION SYSTEMS

2.2.1 The Fordist system of production

In the decades following World War II, prior to the 1970s, the dominant firm structure

in advanced Western economies was that of Fordism. Initially coined to describe the moving assembly line method of mass production employed by Henry Ford's US automobile factories, Fordism refers to an organisational form of production, modelled on Ford's production method, that is characterised by long-run assembly-line production accompanying mass (bulk) production of standardised goods (Sheppard & Barnes, 2003).

The Fordist production model was based upon Fredrick Taylor's *Principles of Scientific Management* (1911). Taylor devised a business process that differed from the industrial revolution's rationally organised mechanised production systems, which involved mechanised subdivided production of standardised products based upon exploitative labour practices, and the unequal redistribution of capital-gains, i.e. workers received minimal pay for maximum effort, with profits being retained by the firm's owner(s) (Besson, 2000; Rupert, 2000; Boyer and Julliard, 2001).

Taylor's business process (Taylorism) was developed through time and motion studies involving disciplined workshop organisation, e.g. tool and implement standardisation, and labour activity subdivision ('parcelisation) through defined task allocation. Taylorism increased production through the parcelisation of labour activities, and the implementation of a wage incentive bonus system to encourage high productivity (Fischer, 2007; Thompson, 2005).

Fordism moved beyond Taylorism, reorganising the entire production process through a greater division and deskilling of manual labour, implementing standardised components in standardised production processes to produce standardised products. The Fordist assembly line method reorganised production by breaking it into many smaller and simpler tasks, i.e. low skilled repetitive tasks that were performed in a specified time period. This 'parcelisation' of the assembly line meant that the rate of production was dictated by the assembly line's speed, a defining characteristic of Fordism, and allowed Fordist firms to employ more unskilled then skilled employees through dramatically reducing the required level of employee training. The assembly line's unskilled nature meant employees could be replaced more easily, meaning Fordist firms' required large supplies of relatively cheap unskilled labour. As such, Fordist firms located production process aspects at (often overseas) locations with cheap labour pools, creating non-autonomous integrated branch plant operations (Oberhauser, 1990;

Delerue and Lejeune, 2011).

All aspects and stages of the Fordist production process, from product design through to marketing and retailing, were conducted in-house, thus facilitating fixed production runs in relation to both the length of the production cycle and the type of product. Due to the scale of production, i.e. large volumes of mass produced standardised consumer goods for increasingly-affluent mass consumer markets, Fordist firms could derive substantial economies of scale by producing inputs internally. This mass production aspect meant that large stockpiles of components were required to prevent input shortages stopping the whole assembly line, which resulted in the development of extensive warehouse management facilities (Capello, 1996; Dicken, 1998; Thompson, 2005).

In order to secure cheap inputs, Fordist firms created dispersed (resource) branch plant operations, again in areas with cheap input costs. Where relationships with outside sub-suppliers developed, they were price-determined contract-based relationships in which relatively little interaction occurred; supply agreements would involve fixed quantities of a particular input, whose exact specifications were determined by the Fordist firm awarding the contract, to be supplied over a certain period of time, after which the process was repeated (Oberhauser, 1990).

The vertically-integrated, hierarchical structured Fordist production processes required a rigidly defined management structure to coordinate the different and sometimes geographically dispersed elements of the production process. As such, Fordist firms were characterised as being bureaucratic and organisationally inflexible (Manicas, 1997; Thompson, 2005).

The Fordist production model predated the Great Depression and World War II, yet both events altered the socio-political landscape of industrialised nations leading to the post-war emergence and dominance of Fordism.

The Great Depression exposed failings in classical (laissez-fâire) economic theory, which had become the prevalent economic model in many industrialised nations following the First World War. Under classic economic theory, government involvement in markets was kept to a minimum which allowed monopolies to dominate the markets.

This resulted in significant social inequality, partly through the suppression of trade unions (Thompson, 2005, Manicas, 1997; Rupert, 2004; New Deal Network, 2003).

In efforts to reverse the Great Depression during the 1930s, the economic theories of John Maynard Keynes gained popularity, most noticeably with then US President Franklin D. Roosevelt. Keynes, in his 'The General Theory of Employment, Interest and Money' (1936), promoted direct government involvement in the management of national economic performance, including the stimulation of economic performance through active fiscal policy based on interest rate reductions and investments in capital goods, e.g. infrastructural investments. Keynes advocated a more equitable redistribution of capital through increased purchasing power to stimulate consumer demand so as to further strengthen economic performance (Thompson, 2005, Manicas, 1997; Rupert, 2004).

Following World War II, partly due to the US government's adoption of Keynesian policies during the war being perceived as ending the Great Depression, Keynesianism became the dominant economic policy of industrialised nations. Keynesian interventionist economic policies complemented Fordism in several ways. Firstly, as an economic philosophy, Fordism/Keynesianism suggested that widespread prosperity and high corporate profits could be achieved by high wages that allowed workers to purchase the output they produced themselves. These high wages were secured through the development of strong trade unions, another Fordist characteristic, whose development was facilitated by Governments seeking to implement their Keynesian policies. High wages meant that the high-output Fordist firms' production levels were matched by the increased purchasing power of their workforce (Manicas, 1997; Rupert, 2004).

Secondly, the Bretton Woods international monetary system, created in 1944 to avoid the economic instability of the 1930s perceived to have created the preconditions of WWII, controlled international trade and finance through fixed exchange rates to minimise international market fluctuations. This meant Fordist produced consumer items were sold in protected domestic markets (Manicas, 1997; Cohen, 2001).

2.2.2 The emergence and development of the Post-Fordist production system

In part, Keynesianism facilitated a post-war period of economic expansion, particularly among industrialised nations, which lasted until the early 1970s. However, a series of

events which emerged in the 1960s, and whose effects subsequently deepened during the 1970s and 1980s, led to Governments replacing Keynesian policies with more neo-liberal open market policies. Additionally, the competitiveness and dominance of Fordism came under increasing pressure and competition (Rupert, 2004; Harvey, 2005).

During this period, a series of global economic shocks exposed the inflexibility of Fordist structures and undermined the effectiveness of Keynesian policies. These shocks caused a protracted period of poor economic performance amongst most industrialised nations, the decline of established industrial areas, and significant market volatility (Rupert, 2004).

The international financial system experienced significant unrest due to fluctuations in currency markets and gold prices, which ultimately caused the Bretton Woods monetary system to collapse in 1971. This resulted in significant market turmoil; a period of high inflation was followed by a global recession characterised by 'stagflation' i.e. inflation combined with economic stagnation and high unemployment levels. Additionally, two oil pricing crises, triggered by the Arab oil embargo in 1973 and the outbreak of the Iranian Revolution in 1978, had significant impacts on global inflation rates during this period (Bruno and Sachs, 1985; Olson, 1985; OPEC, 2000; NESC, 1996; Harvey, 2005).

Leading industrial nations also faced rising competition from foreign markets, e.g. South East Asia, due to economic globalisation; to avail of cheap labour costs, industrial manufacturing increasingly moved to second- and third-world countries, while advanced industrial economies shifted towards knowledge-based service activities facilitated by rapid advances in new information and communication technologies (NICTs). During this period, industrialised nations began entering a post-industrial 'Informational Age' in which information/knowledge began to play a similar economic role as energy/fuel played in the industrial age (Castells, 2000; Acheson, and Lambkin, 2009; Krafft et al., 2011).

Also during this period, increased market fragmentation and segmentation emerged in industrial nations; due to a post-World War II baby boom, and the various social movements from the 1960s onwards, affluent 'baby boom' consumers became increasingly fashion-conscious and demanded more product variety and choice. As

such, market demand and trends became more specialised and altered too quickly for Fordist structured firms to adequately respond to the changing market conditions (Jessop, 2006).

This inflexibility allowed small, innovative information-based Post-Fordist firms to challenge the dominance of Fordism, and gain competitive advantage in key industrial sectors. This development was possible through the emergence of flexible specialised production processes based on the application of NICTs, i.e. applying technologically advanced numerically controlled machines and robots to production process, and the development of flexible organisational forms that facilitated the fragmenting of production processes through outsourcing and the adoption of just-in-time (JIT) delivery systems, which involve suppliers delivering the necessary quantity of specified low-volume inputs to a customer firm's assembly plant on a just-in-time basis

In combination, these elements continue to provide Post-Fordist firms with a flexible manufacturing process. Instead of mass-produced generic products, they have greater ability to respond to rapidly changing market segments by being able to rapidly diversify the type and amount of a product they make to produce diverse product lines targeted at different consumer groups (Dicken, 1998; Oberhauser, 1990; Essletzbichler, 2003; Piore and Sabel, 1984).

Post-Fordist manufacturing flexibility takes different, sometimes interlinking forms, i.e. flexibility within firms, and flexibility through supply-based linkages with outside firms/actors. Flexibility within firms is achieved through intra-firm fragmentation. Instead of a largely unskilled workforce engaged in parcelised production tasks, the different intra-firm operating units of Post-Fordist firms can be organised autonomously, i.e. units may operate in different locations and specialise in producing different components, which are then brought together for final assembly. These units may also have functional flexibility, i.e. they are responsible for numerous production process tasks, meaning Post-Fordist firms utilise combinations of low-skilled workers, e.g. in maintenance and menial positions, and highly skilled engineers and machine operators to oversee their computer automated production processes (Oberhauser, 1990; Vercellone, 2007).

The tendency of Post-Fordist firms towards input externalisation/outsourcing from sub-

suppliers is due to their changing batch production run input requirements. Unlike Fordist firms, the quantities required in their production runs are too small to deliver economies of scale. Yet economies of scale can be achieved through outsourcing, i.e. inputs can be purchased cheaply from a supplier that itself specialises on a particular activity, and by simultaneously supplying a number of client firms achieves economies of scale in its own operations (NESC, 1996).

Subcontracting provides greater flexibility in various areas, including:

- where cyclical or seasonal variations in demand, or demand for a particular product line is insufficient for continuous mass production;
- where firms seek to control labour costs by taking advantage of cheap labour through awarding contracts to the lowest bidders;
- where firms seek to maintain flexibility over variable capital by placing employee benefit responsibilities upon contractors, and subcontract to small non-unionised firms to retain labour process managerial control, and;
- where firms seek to access scarce specialist labour skills (Holmes, 1986; Piore and Sabel, 1984).

Furthermore, outsourcing from specialist suppliers also allows firms greater flexibility in responding to technological changes, i.e. where adopting new production technologies may put efficiency and output at risk, or where the maintenance of older technologies may reduce production capabilities. Essentially, the rapid pace of technological change means it is uneconomical for firms to try and keep up-to-date with development trends, therefore they increasingly rely on specialist suppliers who, due to their narrow activity focus, are dedicated to tracking and absorbing technological advances. For example, firms seek to by-pass the substantial costs of conducting research (e.g. resource, personnel and equipment costs) through sourcing research externally. The introduction of new organisational forms, in particular the JIT delivery system and new forms of logistics informed by NICT developments have facilitated these different forms of flexibility (Harrison, 1994; Capello, 1996; Dicken, 1998; Oberhauser, 1990; Piore and Sabel, 1984).

Rapid NICT developments have facilitated network and strategic alliance developments between firms at an international scale, by removing traditional constraints such as distance. These alliances are managed through sophisticated logistic operations, as firms

seek to co-ordinate and organise diverse production networks among suppliers, subcontractors and distributors (Harrison, 1994; Dicken, 1998).

Post-Fordism has resulted in separate, yet related trends in the spatial division of labour and production organisation, i.e. the spatial dispersal *and* reintegration of production. The spatial dispersal of production has occurred as, unlike Fordism (where a single firm operates and controls the entire assembly line process), the Post-Fordist production process is fragmented, i.e. the conception and execution of production are differentiated on a global scale, causing a deepening division of labour (Capello, 1996; Dicken, 1998).

Additionally, the rapidly changing needs and requirements of Post-Fordist firms means that they have much deeper relationships with their suppliers then Fordist firms, as they will seek to ensure input quality, reliability and supply. This can lead to inter-firm strategic alliances developing, i.e. sub-suppliers themselves outsource work to other sub-suppliers. In some industries, several 'tiers' of sub-suppliers form, which results in the spatial reintegration of production, i.e. horizontal networks of inter-related specialist subcontracting firms which display strong geographic localisation tendencies, as close proximity is required (in part) to respond optimally to the changing demands of client firms. The spatial reintegration of production has resulted in spatial agglomerations emerging, i.e. concentrations of production activities and corresponding labour processes in regional complexes (NESC, 1996; Harrison, 1994; Dicken, 1998; Oberhauser, 1990; Piore and Sabel, 1984).

Over time, due to the high interaction levels, the nature of these relationships may shift from purely commercial market-based relationships, to being based on trust and mutual benefit, i.e. relationships develop past formal contracts. The development of tiers of subcontractors in a particular location can mean that, where trust-based inter-firm relationships develop, they can extend beyond individual relationships to an entire industrial sector (Easton, 1992; Dicken, 1998; Lundberg and Andresen, 2012).

In response to these developments, Fordist firms began restructuring themselves to mirror the Post-Fordist organisational form by introducing fragmented production processes to achieve improved flexibility and higher levels of responsiveness. This restructuring included the introduction of more horizontal management structures, the granting of greater autonomy to operating units, and the increased outsourcing of

material and service input production to independent suppliers (Sabel, 1994; Reich, 1991).

As a result, the operational characteristics of both flexible Post-Fordist and restructured Fordist firms have become increasingly enmeshed in:

> "…*external* networks of relationships with a myriad of other firms: transnational and domestic, large and small, public and private. Such inter-relationships between firms of different sizes and types increasingly span national boundaries to create a set of *geographically nested relationships from local to global scales*…new forms of collaboration are emerging which are embedded within much flatter and looser network structures or webs of enterprise" (Dicken, 1998: 223). (Italics authors own)

The Post-Fordist organisational structure of horizontal alliances of interrelated specialist actors means it is increasingly difficult to clearly define the boundaries of a firm's structure in comparison to the vertical structures and more defined boundaries of Fordist firms (Dicken, 1998; Visser and Boschuma, 2002; Pitt et al., 2006).

2.3 NETWORKS

There are many definitions of networks, depending on the sector being studied. Common elements of these definitions, and key characteristics of networks are detailed in Table 2.1.

Where a region achieves dense inter-actor networks and significant innovative activity, a regional 'brand' can form, making its innovative capacities more visible. Branding strengthens a network's density and capabilities through attracting additional actors, labour and support structures into a region. This enhances information flows, assists actors in building global linkages, and improves the innovative capacities among existing actors and new actors, e.g. new firms set up to pursue new possibilities in terms of new products and techniques (Porter, 1998; Compete, 2005; OECD, 2004; Kolympirisa et al., 2011).

Density can create a more extensive region-specific skilled labour base by attracting and integrating different and related labour skills, expertise and know-how, relative to the network's core activities,
into a local labour market. This reinforces network density, as a specialist labour pool facilitates increased knowledge generation. Where different knowledge is combined, it opens the possibility of vertical and horizontal specialisation "and the development of adequate organisational devices for the integration of...relevant knowledge" (Orsenigo, 2007: 201), thus enhancing the filter aspect of networks (Krugman, 1991; Delerue and Lejeune, 2011).

Table 2.1: Defining characteristics of networks
Networks form when existing stable collaborative commercial relationships shift to trust- and reciprocity-based relationships. This shift occurs through self-organisation, i.e. actors choose to engage in implicit and open-ended co-operative and collaborative transactions/exchanges to secure specific business objectives they cannot achieve through simple bilateral exchanges. Networks facilitate exchanges of resources and knowledge among network members only, and allow advanced specialisation and/or increased operational flexibility.
Networks are either formal or informal relationships, both have restricted memberships: • Formal networks are rigid agreements on common business goals so as to achieve more sophisticated business practices. They involve exchanges of codified knowledge and information, i.e. knowledge/information embodied in machinery and equipment, codified through (for example) patents. Only the members of a network can benefit from these alliances due to their (sometimes) contractual nature. • Informal networks are loose social connections primarily involving knowledge/information transfers through face-to-face interactions. They involve tacit knowledge diffusion, i.e. privately held knowledge/information accumulated by technical and research personnel through practice and experience at the interface between organisations. Such transfers are optimised through geographic proximity and relational norms.
Trust and reciprocity are central and interwoven aspects of how formal and informal networks function: • Trust is a product of the degree and nature of economic relationships in social contexts, which builds and consolidates through members demonstrating their reliability and trustworthiness to each other over a period of time. Networks develop with restricted memberships because of this. Trust determines the willingness/openness of network members to exchange information/knowledge and/or resources by establishing mutual confidence, through a social 'contract', that members will not (for example) exploit vulnerabilities or act opportunistically. • Reciprocity is a mutually contingent exchange of benefits that involves actors reciprocating each other's actions/services. The level of service between actors depends on the level each receives from the other. The importance and intensity of these elements relates to the features of the industry, and the collaborations actors engage in. Both aspects are important in bringing stability in uncertain, technology intensive sectors.
Two principle benefits to networking can be identified; exchanges of resources and knowledge, irrespective of the flows between members. These benefits inform the principle interlinked and/or parallel motives underpinning networks: • Economisation motives, where firms seek to achieve increased flexibility and additional capacity through the division of production activities among members, and to share the costs and/or risks of activities that are too excessive for them to absorb alone, e.g. joint research programmes. • Strategisation allows members to access the technical capabilities of other members, and to augment their innovative capacities by improving their internal competencies and problem solving abilities. Improved response times, flexibility and resilience to evolving markets can be engendered through developing 'resource packages' as a result. It also facilitates codified and tacit knowledge transfers, allowing members access different knowledge bases to improve their capabilities through organisational learning. Furthermore, formal strategic alliances can allow small firms achieve relationship 'asymmetry' with larger firms, improve perceptions of reputation and image, and to address legal and/or regulatory requirements by accessing the resources of other members. Accompanying and underlying these motives, actors seeking to exploit and explore the knowledge bases and resources of other members to achieve improvements, refinements and extensions to their own competences, technologies and paradigms. This can result in innovative developments by allowing actors compare their relative strengths and weaknesses, facilitate increased levels of trust, and encourage the formation of more complex alliances.
Close social relationships among actors in close proximity optimise networks through channelling information and resource within a defined social structure that emphasises trust and reciprocity. Social relationships are vital due to the social character of tacit knowledge transfers and the importance of trust and reciprocity in networks. An area's social customs mean networks are spatially idiosyncratic, while close proximity reduces transaction costs and insecurities, facilitating common cultural rules and routines which limit knowledge group fragmentation and deter harmful actions.
Regional endowments of firms, institutions, and the non-structural underpinnings of behavioural characteristics and social regulations (i.e. the features influencing how actors interact, the nature and character of transactions, and collective learning capabilities) are not homogeneous and can be region specific. Actors can have non-reproducible, regional specific organisational forms/targets that form a local knowledge community or organisational field, which determines the innovative capabilities and development trajectory of a sector.
Networks allow members observe each others internal routines and operating procedures. Those observed as being most efficient and effective are diffused, fine-tuned and replicated among members, gradually becoming accepted routines and procedures. This drives density by facilitating the development of close social relationships and organisational proximity as structural similarities arising through the adoption of organisational forms improve perceptions of trustworthiness among the wider network structure. This is termed mimetic isomorphism.
Regional specific forms and characteristics are influenced by the presence, or absence of a dominant actor type, i.e. the main/largest connected component of a network, whose institutional characteristics influences (formal or informal) networks within a wider network structure: • Networks dominated by (a) commercial actor(s), e.g. manufacturing-based industries, are predominantly formal and codified in nature as such actors derive competitive advantages from possessing advanced forms of resources and knowledge over their competitors. Alliances with external actors are formal and contractual to contain knowledge or innovation developments and exchanges, and to internalise their innovative developments to minimise 'leaks'. The degree of centrality (i.e. the relative trust and geographic proximity) 'junior' actors have to the dominant actor determines their ability to access closed information flows. Centrality makes a dominant actor an obligatory passage point for transfers. Perceptions of trust are therefore crucial, further engraining the formal nature of such alliances. • Networks dominated by non-commercial actors, e.g. public research and education organisations (PREOs), are informal in nature as they are less concerned with market demands. PREO-generated knowledge is spatially 'sticky', due to its predominantly tacit nature, meaning such networks are spatially concentrated. This concentration has deepened due to the importance of information/knowledge in the 'information age', and by government's seeking to engender commercial developments from PREOs through commercialisation supports that create a collaborative environment between commercial and public actors. PREO-based scientific research is increasingly crucial for modern high-tech industries, e.g. biotechnology. The innovative intensity of a region's high-tech firms positively relates to the quality of a region's PREOs and the knowledge they generate. Relative proximity and social inclusiveness to PREOs determines how members engender informal relationships to access commercially related and 'filtered' PREO-based tacit research knowledge. This also impacts on formal networks, as the earlier a technology is licensed, the greater exclusivity firms gain. A regional specific network structure is usually a function of a specific industrial setting, while (paradoxically) the structure and functioning of networks influences the way an industry's technology evolves. Different dominant actors can co-exist in a wider network structure, playing particular roles as a sector develops and evolves. The changing nature of innovation in a maturing industry means that as firms develop, their demands will change, e.g. the dominant actor can shift from an open to a closed actor type due to changing resource needs. Formal arrangements can dominate as technological fields stabilize and innovation becomes less radical.

Based on (Rosenfeld, 2001; Owen-Smith and Powell, 2004; Compete, 2005; Lia and Gengb, 2012; Daskalakis and Kauffeld-Monz, 2007; Simon and Tellier, 2011; Visser and Boschma, 2002; Gertler and Levitte, 2005; Soh and Roberts, 2000; Kogut, 2000; Graf and Krüger, 2011; Chiaroni and Chiesa, 2006; Ahrweiler et al., 2011; Malecki, 1997).

A specialist labour pool can further drive density through facilitating information spillovers, i.e. localised informal knowledge transactions on innovations, production refinements, and business conditions can develop with actors not specifically

included/integrated into a specific network agreement. Spillovers occur where tacit practices and routines mingle with tacit components of knowledge encountered elsewhere through informal and formal networks, e.g. social meetings, and the mobility of local science and engineering labour through research/product alliances (MacPherson, 1998; Feldmann, 2000; Gertler and Levitte, 2005; Engel and Del-Palacio, 2011; Delerue and Lejeune, 2011).

As detailed above, Post-Fordist workers are increasingly involved in the conception and execution of tasks, meaning they develop/generate substantial levels of tacit knowledge, i.e. "the secrets of industry may not be floating freely in the air, but they are situated in informal communities of practice that constitute a local technology labor market" (Owen-Smith and Powell, 2004: 7). Through such interactions, different (codified) knowledge can be combined, facilitating exploitation, and resulting in spillovers which encourage innovative and commercial developments through the assimilation, adaptation or accommodation of the previous practices. This further deepens regional network density (MacPherson, 1998; Owen-Smith and Powell, 2004; Compete, 2005; Kolympirisa et al., 2011).

Such localised informal transactions are key features of knowledge intensive sectors, such as biotechnology, particularly as they encourage new commercial developments and facilitate the formation of collaborative business support services that are tailored to the demands and requirements of the overall network structure. New commercial developments can also contribute to the generation and application of new knowledge, and the development of innovative technologies and products, by stimulating market structure changes and entrepreneurial agreements. Such developments can deliver higher productivity and comparative advantages, and also strengthen a region's competitiveness (Compete, 2005; MacPherson, 1998).

In alliance with support service developments, new commercial developments can boost a region's 'brand'. Essentially, positive feedback events occur which deepens network density and further engrains the non-reproducible, regional specific characteristics of the network's structure. Once network density reaches a certain critical mass, it becomes self-expanding due to the mutually reinforcing or symbiotic relations which develop. Critical mass is a fluid notion, determined by situation and circumstance, yet it refers to a variety of assets that are subject to economies of scale and scope, including

skill-sets, derived from densities of interactions, combinations, learning and innovation processes. Critical mass is important as it impacts on a location's future industrial performance/growth trajectory, e.g. it may increase a network structure's resistance to external and internal forces, such as technological discontinuities (Forfás, 2004; Porter, 1998; Siegel et al., 2003; Anderson et al., 2004).

Yet, differences in actor characteristics, particularly the dominant actor type, can prevent regions developing significant network density or critical mass, i.e. limited actor numbers and market size can inhibit labour mobility and spillovers, limit innovative developments by preventing user/producer interactions, and can also undermine information dissemination (Malecki, 1997; Graf and Krüger, 2011; Eisingerich et al, 2012).

Formal networks are important in such areas, as they can substitute for advantages bestowed by agglomeration. Regional limitations in the supports and resources actors can access, relative to more densely networked and resource endowed regions, compel actors to form alliances with non-local actors in more endowed locations so as to by-pass their regional limitations and to enhance their capabilities and optimise their long term developments, i.e. actors develop alternative forms of proximity, such as 'distant networking' strategies, to by-pass structural weaknesses (Gilding, 2008; Wilhelmsson, 2007; Ozman, 2006; Lundberg and Andresen, 2012; Delerue and Lejeune, 2011).

Yet the effectiveness of such strategies can be limited by the nature of the relationships they seek to develop, and the character of the actor(s) with which they seek to develop alliances. For example, private investor actors typically seek informal alliances with actors located in close proximity due to the importance of information in such alliances. This means that actors from less endowed regions will struggle to engender such relationships. As such, less endowed regions experience cumulative disadvantages, and fall further behind, relative to the more endowed regions (Gilding, 2008; Ozman, 2006; Chen at al., 2011; Morris, 2011).

2.4 INDUSTRIAL CLUSTERS

Geography can significantly impact the form, functioning, and development of networks, as:

- regional endowments of actors, and their institutional and non-institutional characteristics, are not homogenous;
- where close social relationships develop amongst actors in close geographic proximity to each other, the effects/benefits of formal and informal networks may be optimised and emphasised. Proximity can result in trusting relationships developing by facilitating common cultural rule and routine developments, and the adoption of organisational forms that reduce transaction costs and insecurities (through mimetic isomorphism), and;
- critical masses of actors and networks can drive the formation of self-supporting regional agglomerations. This can engrain a region's network structure and sectoral supports, and result in extensive external alliances forming through a branding effect that facilitates access to, and attracts in alternative and international sources of labour, knowledge, resources and finance (Barley et al., 1992; Malecki, 1997; Gertler and Levitte, 2005; Rowley et al., 2000; Huggins et al., 2012).

Where dense agglomerations of networks and actors form, the concept of cluster building may develop among the more interlinked partners. The "…concepts of networks and clusters overlap. A group of firms which network to collaborate…might well be part of a larger cluster" (Cooke, 1996: 21), yet there are noticeable differences between both concepts (see Table 2.2).

Network density can facilitate cluster formation in several ways, primarily through creating the preconditions which result in cluster emergence, particularly through supporting the development of "relationships and routines [i.e. learned, regular and collective patterns of interacting] among the partners…[in which] the capabilities of clusters are found" (Compete, 2005). While networks are important aspects of clusters, cluster emergence occurs due to a wide variety of case and sector specific reasons. These issues are discussed in the following sections.

2.4.1 The concept of industrial clustering

Defining the key characteristics of a 'cluster' is complicated as it is a somewhat nebulous concept. No single unifying interpretation of what constitutes a cluster exists, i.e. there is "no overriding cluster theory per se…clusters are generally viewed as an economic development process rather than a definite development theory" (Brown, 2000: 13).

However, through reviewing a wide variety of cluster definitions, several commonalities can be identified. A cluster can be conceived as a mode of organisation of a productive system that contributes to the innovation and competitiveness of its constituent actors. The linkages between, and the interdependencies/collaborative arrangements among actors are at the core of the concept. Clusters have no membership limits, they are voluntary, non-contractual systematic relationship arrangements based on trust in which actors collaborate and compete to facilitate acquisitions of wider competencies and to build competitive advantage in a local system of specialised sub-supply, service providers and institutes (Rosenfeld, 1997; Porter 1998; Visser and Boschma, 2002; NESC, 1996; vom Hofe and Chen, 2006; Engel and Del-Palacio, 2011).

Table 2.2: Characteristic differences between networks and clusters	
Networks have restricted membership.	Clusters have open membership.
Networks facilitate common business goals.	Clusters facilitate open business goals/shared visions.
Networks facilitate more sophisticated business practices.	Clusters facilitate the acquisition of wider competencies.

Based on (Rosenfeld, 2001; O'Doherty, 1998).

The cluster concept was introduced by Michael Porter in 1990, however the discipline of agglomeration economics has a long history. Geographical concentrations of industries in urban areas have featured in advanced economies since the industrial age.

Alfred Marshall, in his *Principles of Economics* (Marshall, 1890), termed industrial agglomerations 'industrial districts', based on his observations of how related industries concentrated in particular localities in Lancashire and Sheffield, and were typically made up of highly specialised producers in a certain industry exchanging products, which allowed firms to achieve a high level of economies of specialisation (Iammarion and McCann, 2006; Piore and Sabel, 1984; Ingley, 1999; Erden and von Krogh, 2011).

Marshall identified several factors underpinning the processes that determine industrial district formation. These included the development and availability of specialist input suppliers, industry-specific skills, a skilled labour pool that all firms draw from, and the circulation of industry-specific information and knowledge facilitated by a distinct industrial culture and set of norms that regulated firm behaviour, and facilitate inter-firm trust that formed and was optimised by the regional concentration of firms. This meant that the social depth of the firm and the role of governance were important in determining the success of an industrial district (Cooke, 2002; Krugman, 1991; Malecki, 1997; Brett and Roe, 2006; Zhang and Haiyang, 2011; Erden and von Krogh,

2011).

Following Marshall, a wide range of theories focused on industrial agglomerations using different spatial ranges, while some focused mainly on the economic relations that develop between inter-linked firms. However, these theories essentially focused on the same thing, i.e. the benefits which can be derived from groupings of connected or related firms through (for example) customer/supplier relations, competitive rivalry and the development of specialised labour pools. A small selection of these theories is detailed in Table 2.3.

Table 2.3: A selection of industrial agglomeration theories
Alfred Weber's (1909) concept of agglomeration economies: firms derived savings locating in close proximity to other firms within an agglomeration. Weber distinguished between regional location factors, i.e. factors of production availability and transportation costs, and agglomeration factors, i.e. the scale of operations in an area.
Francois Perroux's growth pole concept (1950): a non-spatial theory where groups of firms clustered around central propulsive (related) industries constituted growth poles by undergoing long-term expansion.
Jacques Boudeville's growth centre concept (1960): agglomerations of linked industries concentrate in particular, mainly urban, regions. This was essentially a spatial application of Perroux's concept.
Henderson's (1974) concept emphasised the agglomerative effects of positive spillovers between firms in geographic proximity.

After (vom Hofe and Chen, 2006; McCann, 2001).

The industrial districts concept received renewed interest in the 1970s due to the emergence and considerable economic success of regions dominated by specialist industrial agglomerations of small-firms. These regions were, and remain, associated with high levels of flexibility and innovation, and included:

- the electronics agglomeration of 'Silicon Valley' in California;
- the traditional industry agglomerations of the 'third Italy' region in the Northeast of Italy, centred on the regions of Emilia Romagna and Tuscany, and;
- 'Toyota City' in Aichi, near Nagoya, Japan (NESC, 1996; Owen-Smith and Powell, 2004).

Aside from 'Toyota City', where layers of small subcontracted firms agglomerate around a major client automobile firm, the 'neo-Marshallian Industrial districts' are characterised as highly localised, Small and Medium Enterprise (SME) dominated mono-industrial production systems, where firms specialise in various stages of a product's production, i.e. firms interact through dense networks of sub-contracting, with a highly differentiated division of labour. The presence of long-term linkages between suppliers and end-users, and a sense of community and common interest, enhanced by proximity, create a communal sense of trust which fosters a culture of information-sharing, and learning, and enhances innovation and restricts opportunistic behaviour (NESC, 1996; Visser and Boschma, 2002; Dicken, 2003).

The factors Marshall identified as determining industrial district formation processes remain relevant in the modern era. However the conditions which create such agglomerations have altered somewhat. Many older industrial agglomerations formed due to historic 'accidents', e.g. metal working developing in an area rich in iron ore reserves. While this retains some relevance, today's high-technology clusters are more likely to have developed due to less fortuitous reasons, such as the existence of a pool of highly skilled and specialist researchers, and policy developments (Cooke, 2002; Krugman, 1991; Brett and Roe, 2006; Zhang and Haiyang, 2011; Lee, 2012).

Additionally, differences can be noted between the characteristics which typify traditional and modern clusters/agglomerations. Traditional agglomerations typically formed among horizontally (formally) networked firms operating in the same end product market/industry group. They were characterised as relying on incremental innovation and developments to products and processes. Modern clusters are characterised by different actors in a variety of long-term relationship types, i.e. formal and informal relationships, and are highly innovative as radical innovation processes augment organisational structures and product and process developments. The complex nature of the "internal social dynamics" (Feldman and Braunerhjelm, 2007: 4) of modern clusters separates them from traditional agglomerations (Owen-Smith and Powell, 2007; Enright and Roberts, 2001).

2.4.2 Porter's theory of industrial clusters

The industrial cluster concept was developed by Michael Porter in his *Competitive Advantage of Nations* (1990), through his analysis of the factors determining national competitiveness: "The basic unit of analysis for understanding National Competitive Advantage is the industry. Nations succeed not in isolated industries...but in *clusters* of industries connected through vertical and horizontal relationships" (Porter, 1998: 73). Italics authors own.

Porter initially argued that individual nations gain competitive advantage in particular industrial sectors that compete internationally, and that successful sectors portray strong tendencies to concentrate within particular regions. In a revised edition (1998), Porter adjusted his geographic focus to include non-internationally competitive regional industries. At a national level, Porter conceived clusters as broad industry groups linked within the overall macro economy. At the regional level, the constituent elements share

common regional locations, including urban areas, labour markets, and/or other functional economic units (Porter, 1990, 1998).

Porter defines clusters as "geographic concentrations of interconnected companies, specialist suppliers, service providers, firms in industry, and associated institutions, (e.g. universities, standard agencies, trade associations) in a particular field that compete but also co-operate" (Porter, 1998; 197). The interconnections are characterised by vertical, i.e. supply chain, and horizontal relationships, e.g. the presence of common customers, and technology. The linkages and interdependencies among actors in value chain activities are at the centre of the concept (Porter, 1998; Enright and Roberts, 2001).

Porter focuses on the importance of close proximity in facilitating synergistic interactions between actors that generate innovations. Proximity stimulates innovation by facilitating information/knowledge and technology transfers through repeated trust-based exchanges, i.e. networks. Only through constant innovation, improvement and upgrading, including product, process and organisational methods innovation, can competitive advantage be attained and sustained. The nature and sources of competitive advantage differ widely amongst industries, and cannot simply be equated with economies of scale or labour cost differences (De Witt, 2001).

Porter proposed a 'diamond' (Figure 2.1) of four broad determinants of national competitive advantage, i.e. Factor Conditions, Demand Conditions, Related and Supporting Industries, and Firm Strategy, Structure and Rivalry.

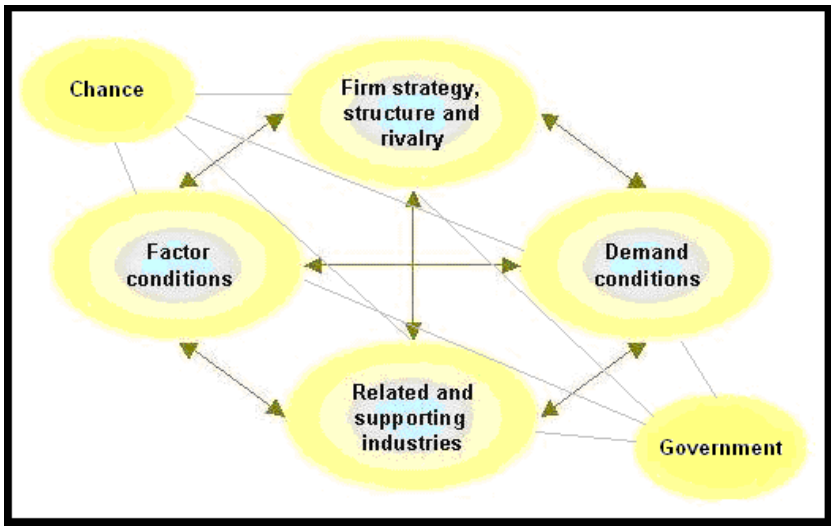


Figure 2.1 Porter's Complete System (After Porter, 1998 and Dagmar, 2001)

The interaction of these determinants, and the influence of two additional factors (Chance, and the Role of Government), create the context, individually and as a system, in which firms are created and compete. Essentially, the 'diamond' is a mutually reinforcing system where the effects and influence of one determinant is dependent on the state of the other determinants, i.e. "...the role of any determinant cannot be viewed in isolation" (Porter, 1998; 99). For example, factor input deployment is related to firm strategy and structure, while a lack of supporting industries might limit a firm's ability to respond to changing market demands.

How the four determinants of the national diamond manifest themselves at a local level reflect the diverse and place specific elements of a nation and its resources. They determine why particular locations develop clusters and others do not, due (for example) to the uneven spatial distribution of resources, and place specific historical traditions and cultures.

The sources of competitive advantage among different industries differ widely. Porter comments that for knowledge-intensive industries, competitive advantage is required in all diamond attributes as the "interplay of advantage in many determinants yields self-reinforcing benefits that are extremely hard for foreign rivals to nullify or replicate" (Porter, 1998; 73). Essentially, where an industry's competitive advantage relies on one or two attributes, its competitive advantage is less sustainable and can be more easily superseded (Rosenfeld, 2000). The determinants and the influencing factors are detailed in Table 2.4.

2.4.3 Cluster policy issues and formulation approaches

Clusters are place specific in character, yet a number of common visible/perceived advantages and features, predominately associated with modern high-tech sectors, of identifiable clusters have encouraged authorities in industrialised nations to develop cluster promotion policies. Among the observed features are identifiable network-related 'hard' and 'soft' benefits (Wolfe and Gertler, 2007; Lee, 2012; Lia and Gengb, 2012).

Observable 'hard' benefits are tangible in nature, and occur through more efficient business transactions, i.e. strategic and economising network-related benefits. Observable 'soft' benefits are intangible, knowledge-based benefits derived from actor interaction, i.e. explorative and exploitative network-related benefits.

Yet, it is important to note that clustering is not an economic development 'panacea' for a variety of reasons. There is much about the concept that is problematic, while introducing cluster elements to industrial development policy/policies pre-empts many fundamental conceptual, theoretical and empirical questions, which impact on cluster policy.

The cluster concept, and what it constitutes, suffers from definitional and theoretical fuzziness. No single definition exists as to what constitutes a cluster in academic literature. Different authors use different features, characteristics, and activity foci of clusters, and various geographic levels to develop definitions. Indeed, Porter's concept, itself, is a highly generic and indistinct. It admits a very wide spectrum of industrial groupings, e.g. clusters can consist primarily of SMEs and/or Transnational Corporations (TNCs), various specialisations, from footwear clusters to biotechnology clusters, different demand-supply linkage types, factor conditions, and institutional set-ups (Porter, 1998; Amin, 1989; Sabel, 1993).

Porter never defines ‘geographical proximity’, and it is presented as a highly elastic term. Clusters are found at different spatial aggregation levels, including large and small economies, rural and urban/metropolitan regions, states, nations and beyond. Additionally, Porter notes that cluster boundaries continuously evolve as new firms and industries emerge, and as established ones shrink or decline.

Porter also comments that boundaries “rarely conform to standard industrial classification systems” (Porter, 1998: 204), yet even when they do, standard classifications can fail to capture many important aspects, e.g. inter-industry linkages. This geographical fuzziness means there is an almost unlimited scope to the concept's definition and application (Porter, 1998; Martin and Sunley, 2001).

Ffowcs-Williams (2000) comments that these ambiguities prevent precise empirical delimitation that restricts the development of a suitable cluster identification methodology. Indeed, no agreed approach for identifying and mapping clusters exists, in terms of the key variables that should be measured, or in relation to the procedures to determine the geographical boundaries of clusters. This methodological 'fuzziness' directly impacts on cluster policy formulation and implementation (vom Hofe and

Chen, 2006; Martin and Sunley, 2001).

Table 2.4: The four determinants and the two influencing factors of the national diamond

Factor conditions: Traditional economic theory states countries have different endowments of land, labour, capital, and infrastructure. Porter notes these factors now play more complex and complicated roles, i.e. competitive advantage is determined by how they are created, upgraded and made more specialised to a particular industry, as traditional disadvantages can be mitigated through outsourcing. Nations now create factors of production through processes determined by country specific social and political values, and the influence of history. Factor creation requires continual investment and innovation to upgrade and improve them so as to optimally meet the particular needs of a nation's industries.

Porter groups these factors into five general headings:

- the quantity, cost, work ethic and skill sets of human resources;
- the quality, cost, abundance, and accessibility of physical resources relative to other nations;
- the knowledge resources (i.e. stock of scientific knowledge) in PREOs, trade associations, and government agencies;
- the amount, variety and cost of capital resources, as idiosyncratic differences remain between countries despite market globalisation, and;
- the type, quality, and cost of a country's infrastructure, e.g. communications infrastructure, and cultural institutions.

Porter states there is a hierarchy, relating to the industry activities factors are used in:

- Basic and generalised factors, e.g. natural resources and semi-skilled labour, are possibly inherited factors support rudimentary types of competitive advantage, require modest private and social investments, and can be easily nullified.
- Advanced and specialised factors, e.g. digital data infrastructures, are crucial in securing more durable competitive advantage, they require sustained private and social investments in human and physical capital, and facilitate constant and sustained factor upgrading and innovation. Advanced factors are often specialised factors, though not exclusively.

Demand conditions: the nature and character of a home market's demand for an industry's product/service determines competitive advantage by influencing economies of scale, conferring static efficiencies, and shapes the rate and character of innovation and improvement among firms. Porter identifies three key features:

- the composition, segment structure, and nature, mix and character of home demand: despite globalisation, a home markets demand composition can disproportionately affect how companies perceive, interpret, and respond to buyer needs, particularly where sophisticated and demanding buyers require high quality, feature and service standards;
- the size and growth patterns of domestic demand facilitate economies of scale, or learning through increased information dissemination, which can persuade firms to enter a market, and existing firms to invest in facilities and technical developments. Early market saturation, resulting from home demand developments driving foreign markets to react, also forces firms to innovate/upgrade due to increased demand for performance and features, and;
- the internationalisation of domestic demand. Where domestic buyers are mobile and/or transnational, the local market is essentially comprised of domestic and foreign buyers, e.g. TNCs typically remain loyal to domestic suppliers by using the same inputs in all areas of their operations. This presents local supply firms with opportunities to sell abroad. Also, foreign workers entering industrial/scientific training placements transmit domestic needs and/or requirements to foreign buyers through a 'learning from others' effect. This transfers local approaches, values and skills to foreign markets.

Related and supporting industries: the principle tool in understanding and determining competitive advantage is a sector's value chain. This refers to how the performance of one firm-based activity influences the cost or effectiveness of other activities. Inter-related activities often create trade-offs, such as institutional/transaction costs, and require coordinated logistic activities and supply chain management. Where close geographic and institutional proximity exists, linkages with supply firms can be managed optimally. Proximity and cultural similarity facilitates open information flows, reduces transaction costs, improves the perception of new opportunities, allowing firms to develop joint-activities which increase the rate and pace of innovation and upgrading. The presence or absence of internationally competitive suppliers or industries directly and indirectly influences competitive advantage. Suppliers that achieve competitive advantage themselves can confer advantages to customers. Buyers can gain quick insight into and can access information on supply developments, thereby influencing supply firm developments. Exchanges can lead sellers to form joint problem solving and R&D programmes that enhance product/process innovation and upgrading for suppliers and buyers, yet they must actively engage in such exchanges.

Firm strategy, structure and rivalry: The conditions governing how companies are created, structured, and managed, varies among nations, as does the nature of domestic rivalry. These determine competitive advantage, as inter-firm competition drives cluster development. Firm strategy is determined by the nature of firm ownership, i.e. public or private ownership, which is influenced by the nature of corporate governance and the ownership of debt. A public firm reflects the idiosyncratic characteristics and influences of national public capital markets, which have different goals for different industries and remain important despite capital market globalisation, while the goals of private firms are derived through complex factors, such as pride and the desire to succeed in business. Inter-firm rivalry impacts on domestic innovation and drives firm creation through generating demand for related industries, leading to cost reductions and increased demand for new and improved products and processes, and opening market segments established firms may not have observed or considered.

Influencing factors on the diamond:

- Chance developments have little to do with a nation's circumstances, and are outside the control of firms and governments, e.g. technological discontinuities, external political developments, and foreign demand shifts. They cause competitive advantage shifts, altering diamond conditions by reshaping or unfreezing industry structures through discontinuities, while also creating opportunities for a nation's firms to supplant one another. Chance does not mean an industry development is unpredictable, as apparent chance occurrences can exist due to national environment differences. Nations with a favourable diamond will convert chance events into competitive advantage via an environment that exploits new/potential competitive advantage sources.

Government influence the determinants, which themselves can influence policy. Governments cannot be fully aware how all policies impact on a diamond, yet they should be aware of possible impacts. Policy either supports and reinforces competitive advantage, or produces results contrary to their intended impact(s), typically by being poorly designed.

After (Porter, 1998; De Witt, 2001; Lee, 2012; Brett and Roe, 2006; Visser and Boschma, 2002; Europa, 2003; Lundberg and Andresen, 2012).

'Traditional' top down industrial development policies typically emphasise infrastructural investment, and the provision of firm supports and incentives to stimulate sectoral activity,

e.g. to attract TNC Foreign Direct Investment (FDI) and/or facilitating developments among existing firms. While such approaches can play a role in developing agglomerations, the complex influences of chance and serendipity in a cluster system's development and emergence limits the ability of such policies to fully account for unpredictable occurrences, and unintended policy impacts. This does not mean policy is inconsequential, as chance/serendipitous events occur within a limited historical and geographical context, i.e. without suitable conditions being in place, chance events won't engage with existing elements (Brown, 2000; Anderson et al., 2004; Orsenigo, 2007; Feldman and Francis, 2002).

Due to these issues, critics of cluster policies contend that Governments, in seeking to develop the observable 'hard' and 'soft' benefits associated with clusters, often derive measures from 'snapshots' of successful clusters and their sectors. Such an approach is problematic as clusters are unique due, for example, to their socio-cultural, historical, and spatial specificity, and also due to the evolutionary processes which influence their internal structures and development. In essence, 'snapshot' policies isolate a cluster from its economic landscape, ignore other forms of regional and local economic development, ignore the dynamics of the inter-regional system as a whole, and ignore the evolutionary trajectories, interdependencies and dynamics of firms inside a cluster relative to those outside (Martin and Sunley, 2001; Amin, 1989; Sabel, 1993; Staber, 1996; Malecki, 1997; Lia and Gengb, 2012).

Deriving policies from initiatives found in successful clusters also fails to acknowledge that many initiatives promoting clusters often have long histories predating explicit cluster development strategies. Rosenfeld (2002) notes that policies can play a role in agglomeration developments, yet often such policies are rarely implemented with the intent of starting a cluster (Scott, 2007; Kenny and Patton, 2007; Carlsson, 2007; Lia and Gengb, 2012).

Martin and Sunley (2001) comment that clustering has become a 'chaotic concept' due to the variety of meanings and connotations governments associate with it. In part, this issue is due to the concept's definitional and methodological fuzziness, but it is also due to a limited understanding of the concept's fundamentals among public actors. This is reflected in governments introducing 'cluster' policies to promote political strategies, such as decentralisation programmes, and not as economic development tools.

Additionally, policies have been applied at unsuitable geographic levels due to political pressure to avoid offending regional interests. For example, the Sainsbury report on Biotechnology clusters in the UK (DTI, 1999) identified clusters in almost every UK region, even though many lacked key/fundamental features of clusters (vom Hofe and Chen, 2006; Enright and Ffowcs-Williams, 2001; Asheim and Coenen, 2004).

Governments also predominately associate clusters with high-technology, knowledge-based economic activities**,** i.e. industries with a high dependence on knowledge generated and contained in industry- and PREO-based research laboratories, and whose labour skills, technological know-how, and innovative activities are optimised through geographic proximity. However, it is unlikely that all regions can rely on the same knowledge-intensive sectors, as the benefits realised from clustering appear specific to certain industries, and are only realised under particular conditions (Martin and Sunley, 2001; Audretsch and Feldman, 1996; Audretsch, 1998; Keeble and Wilkinson, 2000; Glasmeier, 2000; Ahrweiler et al., 2011; Lee, 2012).

Indeed, Amin (1989) questions whether new clusters can develop through public or private sector intervention in locations where a few basic conditions required for cluster formation are found. Effectively, cluster policies are unlikely to successfully create 'new' clusters in poorly endowed regions, and are more appropriate where a diverse economic base that can support new markets and diversification already exists (Feldman and Braunerhjelm, 2007; Maggioni, 2007; Wolfe and Gertler, 2007; Morris, 2011; Ahrweiler et al., 2011).

Critics also contend that governments seem unaware that cluster policies can actually introduce and embed regional vulnerabilities through promoting a specialised economic activity focus. Uzzi (1997) comments that the processes which create embeddedness develop due to a 'specific' cluster environment, and that sources of inertia and inflexibility, i.e. 'lock-in', relative to firms and industries outside a cluster, can develop over time. Essentially, the same processes which facilitate cluster formation may paradoxically reduce a cluster's ability to evolve and/or adapt to system shocks. Examples of cluster induced 'lock-in' are presented in Table 2.5 (Forfás, 2004; Porter, 1998; Silvia, 2009; Malecki, 1997; Howells and Edler, 2011).

Cluster policies can also reinforce regional inequalities, particularly where they are implemented uniformly (spatially), as more resource and competence rich locations will

better absorb resource investments, relative to less endowed locations, due to their greater capacity levels (Morris, 2011).

Table 2.5: Examples of cluster induced 'lock-in'
• a cluster with a specialised focus becoming resistant to new and different information sources which differ drastically from its established core skills, expertise, and/or supplier bases, i.e. its established paradigm; • the development of a high skilled specialised labour pool driving out lower skilled jobs and firms, which potentially creates an inability for the cluster members to react to external shocks and/or technological changes, and; • where a cluster relies on the activities of a large firm, the cluster may fail if the dominant actor moves from the system, even if it remains competitive.

After (Martin and Sunley, 2001; vom Hofe and Chen, 2006; Ingley, 1999; Eisingerich et al, 2012)

This issue relates to the 'innovation paradox', as identified by Oughton et al. (2002). Such a paradox emerges where actors in poorly endowed regions do not (and cannot) engage in significant innovative activities as they typically underinvest in R&D, which means they cannot (and do not) engage in significant innovative activities. Such actors would also lack an interactive learning tradition due to an established absence of inter-actor cooperation caused, for example, by the presence of 'closed' vertically structured dominant actors and/or the prevalence of conservative business models, which would undermine potential opportunities to exploit synergies and facilitate spillovers (Asheim and Isaksen, 2002; Anderson et al, 2004; Giesecke, 2000; Leydesdorff at al., 2002; Morris, 2011; Eisingerich et al, 2012).

Due to these definitional, conceptual and methodological issues, it is tempting to conclude that the notion of clusters, ultimately, has no real significance for policy measures. Yet, Brown (2000) comments that clusters should be viewed more as an economic development process rather than a definite development theory.

Effectively, the cluster concept can be conceptualised as an umbrella term, or 'brand', which Governments can apply to different aspects of economic activities in different manners. The brand, at its core, is based on an image of a highly productive, knowledge-rich, decentralised, entrepreneurial and socially progressive economy, rather then as a coherent and carefully defined set of ideas and practices. Using the cluster 'brand' as a policy focus can engender better coordination between different policy themes relating to cluster development, while initiatives can be optimally tailored towards regional specific processes and developments by orientating all relevant stakeholders towards cluster development, thus (for example) minimising the introduction of 'lock-in' events (Martin and Sunley, 2001; Wolfe and Gertler, 2007; Graf and Krüger, 2011; Howells and Edler, 2011).

Porter (1998) and other commentators argue that cluster policies should be geared to industrial sectors, and should avoid firm-specific actions in favour of a systems-based approach, as individual firms, for example, are part of a larger industrial system. A systems-based approach is also required as innovation does not occur in a chain link development process, but occurs through multiple reciprocal relationships at different stages of the innovation process between different public and private actors, and different sector segments (Brown, 2000; Anderson et al., 2004; Wolfe and Gertler, 2007; Giesecke, 2000; Orsenigo, 2007; Feldman and Francis, 2002).

Essentially, it is the process by which clusters form and emerge, not the final 'result', which is important in relation to policy measures. This means that policies can be developed to facilitate cluster development in the long-term by being used in a facilitator role, and not as a constructor. The rationale behind this approach, which is detailed further in the following sections, fundamentally differs from top down 'snap shot' derived policies (Anderson et al., 2004; Martin and Sunley, 2001).

Through a review of various cluster case studies from different countries, industries, and Governments, two broad cluster development and evolution stages can be identified, as detailed in Table 2.6. It must be noted that this 'divide' is simply for presentation purposes only, as the border between both stages is fluid.

These stages directly influence the approach, formulation and implementation of cluster policies. As such, two broad approaches to cluster policies can be detailed:

- cluster-specific strategies, which are designed to facilitate 'new' cluster emergence in an area where one does not exist, or has not yet emerged, and;
- cluster-informed strategies, which are introduced following a clusters emergence to optimise its development trajectory.

2.4.4 Cluster specific policy themes

Where Governments seek to develop a cluster where one has not formed/does not exist, their policy approach is termed 'cluster specific'. Such policies challenge conventional thinking about how national, regional and local governments promote economic development and prosperity, particularly where characteristic aspects of cluster systems are not present (Brown, 2000; Anderson et al., 2004; Wolfe and Gertler, 2007).

Table 2.6: Proto-cluster emergence and development stage themes

The processes facilitating cluster development are complex and region specific. Economic systems evolve over time, through complex and idiosyncratic "processes of construction of competencies, supporting institutions, [and] organisational structures" (Orsenigo, 2007: 204), under variable natural, cultural, social and economic conditions "shaped and constrained by past decisions, chance events, and accidents of history" (Wolfe and Gertler, 2007: 244), and which involve complex inter-actions of heterogeneous public and private actors.

Proto-cluster (PC) developments are determined by the factor pre-conditions and seeds which exist prior to their emergence. There is a subtle difference between these elements:

- Pre-conditions are a region's specific, non-reproducible asset base, including its accumulated local stock of knowledge, experiences, resources, institutions and infrastructures, which form prior to a PC's evolution (examples include naturally occurring factor endowments, such as existing ore reserves, and an area's climate, quality of life and living conditions), and the presence of existing agglomerated competences in similar or related industry/industries that actors in emerging sectors can exploit.
- PC seeds/seedings are assets introduced to an area through deliberate actions by actors, such as (though not limited to) Government actors. Seeds can form due to intended impacts from intentional acts, or due to unintentional impacts from deliberate acts.

Pre-conditions and seeds facilitate cluster emergence, yet are not sufficient to solely facilitate cluster emergence.

Cluster emergence is determined by complex processes building upon and priming pre-conditions and seeds, i.e. a trigger process, and a critical mass of entrepreneurial and innovative activity which directly leads to a cluster's emergence, i.e. a trigger event. Both part of the same process, and are presented here separately for explanation purposes only.

PC trigger process: As a cluster is a system. Different feedback forms develop at different points, and at different stages of a trigger process. Feedback determines a cluster's nature and character forms. A PC's trigger process is determined by the nature and character of a system's path dependence and development trajectory, and the presence of inter-actor knowledge/information spillovers;

- PC system path dependence and development trajectory: development trajectory is determined by established cumulative formations, interactions and trade-offs of various hard and soft infrastructures, resources, skills, and actors. Strong associations exist between past investments in hard and soft infrastructures and a system's economic performance, while existing structures and routines mean rigidities and trajectories prevail in innovations. These elements form a system's path dependence, influencing and determining the innovative capabilities and resources of actors. Path dependence influences systemic spillovers by impacting on the interactive environment in which actors operate, meaning it determines and influences the generation, filtering, and dissemination of information. For a cluster to emerge, positive externalities must occur during a trigger process to build upon existing systemic strengths and to address systemic weaknesses. Key determinants of such externalities are entrepreneurship and innovation, i.e. new firms, products and processes which create positive feedback that addresses lock-in and technological discontinuities, which is facilitated and determined by the presence of skilled labour and an entrepreneurial support 'ecosystem' that both facilitates and encourages innovative developments. The factors characterising an ecosystem are fundamentally linked, and are strongly influenced by a PC's pre-conditions/path dependence, and development trajectory. Different supports play different roles in the technological and regional dynamics of a PC, yet they are "mutually determined in a complex web of circular cumulative causation" (Feldman and Braunerhjelm, 2007: 10) which continuously alters through system specific feedback.
- Information spillovers: A cluster's competitive advantage is determined through its value chain, which means a key factor determining cluster emergence is how actors in a system interact. Where localised knowledge transactions occur through informal and formal networks, combinations of tacit practices and routines with new knowledge components facilitate information spillovers. These determine, and are fundamentally determined by the characteristics of a PC system's actors and their networks. Spillovers, particularly where positive pre-conditions/seeds exist, drive a PC's development trajectory through positive feedback inputs, and encourage innovative and entrepreneurial developments that drive network density and facilitate complex networking arrangements through mimetic isomorphism.

PC trigger event: A trigger event occurs through the formation of a critical mass of entrepreneurial and innovative activity that emerges through a PC's trigger process. Critical mass develops over an extended period of time, and depends on the nature and character of a system's support ecosystem and information spillovers. A trigger event's character determines the nature of a cluster's structure, and influences the entrepreneurial and innovative features of its constituent actors and their business structures. Three principle categories can be identified:

- Spontaneous trigger events occur in an absence of policy interventions through local actors proactively seeking to exploit actual and/or potential synergies in a PC's system. Actors proactively organise, i.e. they move away from spontaneous forms of agglomerated interactions towards a more organised and co-ordinated territorial system whose internal functions stratify organically. Such clusters are characterised as being intensely entrepreneurial and innovative in nature.
- Trigger events can occur through (direct and indirect) policy interventions that seek/facilitate a system's emergence through creating an entrepreneurial and innovative support ecosystem that facilitate spillovers and the development of a positive development trajectory.
- hybrid trigger event processes occur through a mix of spontaneous and policy driven developments. Hybrid systems initially form through proactive actor driven developments, yet later experience significant positive systemic inputs due to direct or indirect policy actions which ultimately facilitate a cluster system's emergence.

Due to the 'constructed' aspects of planned and hybrid clusters, their entrepreneurship, innovation activities and internal organisation are less aggressive in nature then spontaneous systems.

A cluster's long-term sustainability, i.e. how it extends and consolidates its competitive advantage(s), is determined by its system being subject to a continual, structured and self-reinforcing process of growth and development through on-going innovative and entrepreneurial activities. Due to the case specific nature of clusters, few cluster emergence and development themes can be detailed. However, two key interlinked determinants of a cluster's long-term positive development trajectory can be identified:

- Second generation (spin-off) firm developments occur in the context of an established innovative and entrepreneurial culture and ecosystem that proactively encourages and facilitates entrepreneurial developments by lowering entry barriers and addressing risk perceptions associated with new developments. The skills and experiences of first generation firms act as reservoirs of knowledge relating to successful firm development, which encourage and facilitate second generation developments, shaping them through mimetic isomorphism. This allows spin-off firms to access existing supports, as they are perceived as system 'insiders'. Spin-out firm innovations are typically path-breaking, and open new sub-markets due to their origin. This drives a system's positive development trajectory by adding to its asset base, deepening networks, and facilitating systemic externalities and spillovers.
- Non-local actors enter a system to access/exploit its highly developed support ecosystem, particularly after the development of spin-out firms. They facilitate increased spillovers through mixing new and old competences. Yet, spillover effects differ for new and existing actors. Existing actors predominately engage in incremental innovation based on an existing paradigm, while new actors are likely to drive radical innovation (which indicates a technological discontinuity for established actors). By increasing systemic activity and engendering positive feedback, new technological upsets are absorbed by both new and old firms, resulting in the improved technological capabilities and depth of the entire system. Such developments can address technological/trajectory 'lock-in', enhance a system's entrepreneurial and innovative 'brand', increase a system's depth and density, and attract in additional actors and their embedded tacit skills, competences, and resources, from less asset rich systems.

After (Cooke, 2002; Owen-Smith and Powell, 2004, 2007; Wolfe and Gertler, 2007; Carlsson, 2007; Romanelli and Feldman's, 2007; European Commission, 2006; Porter, 1998; Gertler and Levitte, 2005; Scott, 2007; Kenny and Patton, 2007; Zhang and Haiyang, 2011; Graf and Krüger, 2011; Eisingerich et al, 2012).

Government policies fall between these two broad approaches, meaning the nature and character of cluster policies ultimately depends on what Governments wish to achieve (Feser, 1998; Brown, 2000; Wolfe and Gertler, 2007).

Cluster policies should be tailored towards building on pre-existing competences and productive systems, which may be embryonic or latent, in a specific sector, rather than aim to create new systems, as "without the presence of underlying national circumstances...the best policies will fail" (Porter, 1998: 617). Additionally, key features of a cluster's internal structure, and many of the determinants of a cluster's development and emergence, cannot be developed solely through policy actions, e.g. the inherent trust-based nature of networks (Malecki, 1997; Scott, 2007; Anderson et al., 2004; Wolfe and Gertler, 2007).

A PC's formation is a long, complex and dynamic process. Porter (1998) notes that numerous studies suggests cluster emergence can take decades, e.g. Silicon Valley's foundations formed in the 1930s, yet it flourished from the 1960s onwards. This means that no one policy, or series of policies, can fully account for a system's evolving nature, i.e. cluster specific policies must develop and evolve over sequential processes, and be adaptive and highly responsive in nature so as to create the conditions which facilitate, support and reinforce a PC system's positive development trajectory (Porter, 1998; Maskell and Kebir, 2005; Scott, 2007; Anderson et al., 2004; Wolfe and Gertler, 2007)

Yet, a decade is an eternity in politics, as demonstrated by 'traditional' industrial development policies, which typically seek short term benefits to fit election cycles. This approach can retard innovation in the long-term through, for example, introducing systemic 'lock-in'. As such, cluster specific policies must transcend short-term business cycle approaches, as "...the most potent influences of government in advanced nations are often slow and indirect" (Porter, 1998: 619; Carlsson, 2007; White, 2000; Graf and Krüger, 2011).

The complex interlinked nature of the themes which facilitate a PC's emergence means a suitably complex policy framework is required to address the relevant policy themes, particularly technology and industrial themes, as a whole, and in a coherent/convergent manner. Optimally, such a framework involves direct interventions to target the creation of required infrastructure and resources, e.g. regulatory initiatives to support entrepreneurship, and indirect interventions which play a facilitator role, e.g. market research assistance and prototype testing (vom Hofe and Chen, 2006; Europa, 2003; Oughton et al., 2002).

Scott (1997) states that cluster specific policies should focus on micro-economic measures, as within "...successful clusters there is a degree of self-organisation that...reflects an underlying complex social process. If policies fail to understand the dynamics of clusters emergence...[there is a significant] risk that a nascent cluster will decline" (Scott, 2007: 11). Additionally, Governments are often directly removed from market forces, meaning policy measures are at best reactive, addressing issues some time after their emergence (Breschi et al., 2001; Anderson et al., 2004; Eisingerich et al, 2012).

The geographic 'borders' of cluster systems are often larger, or smaller, then Geographic units of governance. As such, existing Government and non-Government institutional structures and jurisdictional boundaries may inhibit suitable policy developments by failing to capture key aspects of a PC system's internal dynamics. Indeed Porter (1998) comments that as the basis for competitive advantage is often locally concentrated, "the role of state and local [regional] government is potentially as great or greater" (Porter, 1998: 622) than National or Federal government in developing tailored policies, by being relatively more attuned and responsive to a sector's needs (Steiner, 1998; Brown, 2000; Wolfe and Gertler, 2007; Europe Innova, 2008).

Additionally, close co-ordination between the regional branches of development agencies and local authorities is also required for a uniform policy approach towards industrial and economic development. Yet, in the context of their typically limited resources, it is unrealistic to expect local and regional authorities to be able to fully detect how a PC system develops due to its complex and evolving nature, or to continually anticipate changing service requirements (Ffowcs-Williams, 2000; Wolfe and Gertler, 2004; Giesecke, 2000; Krugman, 1991; Anderson et al., 2004; Eisingerich et al, 2012).

As such, to combat information weaknesses and to tailor suitable initiatives for a PC system, the formulation and implementation of cluster specific policy/policies should optimally involve the key public and private actors in a particular system, through a system-specific actor council or organisation. Essentially, this entails the development of a distinctly new cluster-specific associative governance structure that includes all relevant stakeholders in a PC/cluster system that influence, or may be affected by cluster activities, including:

- National, Federal, Regional and Local government;
- Development agencies;
- Small and large firms in the specific sector, including SMEs and TNCs, and service provides;
- Local PREOs;
- Chambers of Commerce, Industry and Trade Associations, and enterprise boards, and;
- Speculative investors, including venture capitalists (VCs) (Anderson et al., 2004; White, 2000; Asheim and Coenen, 2004; Cooke, 2002).

Integrating a system's public and private actors and institutions into policy decision processes can be a significant challenge for highly-regulated/vertically structured Governments. Yet, such a process is required to optimally tailor initiatives to the specifics of a sector, by establishing a socio-economic dynamic that is based on open discussion and consensus-building through a complex range of interactive settings (including working groups, seminars, interviews, audits and surveys) so as to identify weakness, build on strengths and avoid laziness/complacency. Due to the evolutionary nature of a PC's system, this collective dialogue must be both continuous and open to new stakeholders to join and influence, so as to optimise a system in the context of current and future trends (Anderson et al., 2004; Wolfe and Gertler, 2007; Ffowcs-Williams, 2000; Giesecke, 2000; Eisingerich et al, 2012).

Such elements can be facilitated through introducing a systems integrator, i.e. an actor, or council of key actors recognised by a system's actors, to manage and coordinate the dialogue. An integrator actor/council facilitates the formation of a 'cluster consciousness' by stimulating a sense of communal ownership among actors, aligning the various interests of the different stakeholders, and/or discouraging opportunistic acts which would result in the process' fragmentation. Additionally, a consensus driven dialogue removes/reduces the effect of election cycles on policy developments, and maintains and encourages private sector involvement in a PC's development (Europe Innova, 2008; Ffowcs-Williams, 2000; Maskell and Kebir, 2005).

A suitable systems integrator actor/council crucially creates confidence among the various stakeholders during the early stages of a dialogue process, and also prevents the development of a weak or exclusive leadership, e.g. an elite few which prevents new

members entering the process. An integrator actor/council also addresses complacency due to cluster success, and prevents vested interests or dominant actors, such as monopolies, placing pressure on Governments to protect an existing paradigm which may become outmoded due to new innovative developments. Essentially, it is important that all stakeholders focus on the long-term facilitation of innovation and entrepreneurship, regardless of the 'costs' and system shake outs which may occur, so as to avoid negative feedback inputs/systemic 'lock-in' events forming in the system (Giesecke, 2000; Europa, 2003; Porter, 1998; Casper, 2007; Graf and Krüger, 2011).

A public/private consensus is important for a PC's evolution in relation to the nature of its trigger event, i.e. a PC system's modus operandi should be more in keeping with the private sector with regards to the regulations and conventions governing the operation of capital markets, forms of corporate governance, R&D, and other relevant factors. Private sector actors, ultimately, must be the dominant investors in a system's development, resource and finance wise, and should therefore have a substantial input into the formulation of policy measures (Anderson et al., 2004; Rosenfeld, 1997; Martin and Sunley, 2001; Wolfe and Gertler, 2007; Oughton et al., 2002; Lundberg and Andresen, 2012).

Therefore, Porter (1998) comments that direct government policy intervention(s) into a PC system, sidestepping private actor involvement, should occur only in specific instances, as detailed in Table 2.7.

2.7: Instances when direct government policy intervention(s) should occur in a PC system
Market failures: where a market underperforms and cannot address these issues independently, policies may be introduced to motivate specific system developments, e.g. increased public R&D spending, while alterations can also be made to public procurement policies.
Government policy failures: where an existing policy or policies cause system weaknesses, e.g. the presence of underdeveloped PREOs.
Systemic failures: where structural inconsistencies/mismatches develop between interrelated institutions or organisations, e.g. poor Government jurisdictional and/or agency coordination.

(Metcalfe, 1995; Porter, 1998; Howells and Edler, 2011).

2.4.5 Cluster specific entrepreneurial and innovative functional resource themes

The long-term challenge for cluster specific initiatives is to facilitate the emergence of a competitive, internationally focused PC system through seeding and developing the necessary elements that facilitate a positive trigger process, and ultimately the development of a trigger event. A complex approach is required to introduce the relevant 'hard' and 'soft' infrastructures, skills, resources and supports. Essentially, a support 'ecosystem' that facilitates and drives entrepreneurial and innovative developments throughout a PC system should be sought, one which optimally builds upon strengths, and

addresses weaknesses present in the four determinants of competitive advantage (Feldman and Braunerhjelm, 2007; Porter, 1998; Anderson et al., 2004).

Due to the unique characteristics of PC systems, and also in the context of the issues of deriving 'snapshot' policies from established cluster systems, the following sections do not prescribe a series of detailed policy actions, but detail five inter-connected entrepreneurial and innovative functional resource (EIFR) requirements that have been identified through a review of international cluster and PC case studies, and which draw from Anderson et al. (2004). The EIFRs are:

- Knowledge infrastructure, resources and skills (EIFR 1);
- Entrepreneurial infrastructure, resources and skills (EIFR 2)
- Inter-actor networks (EIFR 3);
- Market information exchange resources (EIFR 4), and;
- Actor and institutional density, and skill, competence and resource depth (EIFR 5) (Ffowcs-Williams, 2000; Casper, 2007; Anderson et al., 2004; Carlsson, 2004).

The EIFRs facilitate the development of a PC system's 'ecosystem' that feed into the development of the four determinants of national competitive advantage. They also represent the key themes around which a PC's public/private dialogue process, and the formulation of cluster specific policy initiatives, should be orientated.

Prior to the formulation of cluster specific initiatives, a formal mapping exercise, i.e. a Strengths, Weaknesses, Opportunities and Threats (SWOT) analysis, is required to identify the idiosyncratic sectoral/system strengths and weaknesses, and to identify opportunities to exploit a PC's pre-conditions and seedings. Such an analysis is best viewed as a general mode of inquiry, rather then a narrowly defined regional economic analysis whose methodology is dependant on particular policy concerns. Optimally, a PC should first be studied in spatial isolation from the general economy, to shed light on actor and institutional interdependencies. It should then be analysed in its spatial context in relation to a larger (external) economic unit of which it is part, i.e. state or nation, so as to place it in its proper context as to how it is embedded into the local economy (vom Hofe and Chen, 2006; Wolfe and Gertler, 2007; Rosenfeld, 2000; Eisingerich et al, 2012).

A PC's strengths are its existing resources and capabilities which form the basis for

developing competitive advantage. Its weaknesses are essentially the absence of certain characteristics that place it at a disadvantage relative to other systems, examples include patent protection strength/weaknesses, and the system's ability/inability to react to market changes/shocks. A PC's opportunities and threats are external issues which can impacts on a system's competitive position, examples include technological and/or market change, and changes in the marketplace or competitive position (Wolfe and Gertler, 2007; Rosenfeld, 2000; Zhang and Haiyang, 2011).

A SWOT analysis should also inform the development of a public/private dialogue process, and the development of supports to encourage pro-active private sector involvement in a PC system's development. A SWOT analysis provides policy makers with a better understanding of how a local economy is structured, and can assist in the formulation of direct 'accelerators' to re-equilibrate the identified system before initiating cluster specific initiatives. Examples of 'accelerators' include the development of key infrastructure elements, such as up-to-date telecommunications and NICTs, and suitable transport links (Ffowcs-Williams, 2000; Porter, 1998; Orsenigo, 2007)

Additionally, it is crucial that supports are developed to encourage private sector involvement in a PC's development, particularly where private actor innovation and/or investments are restricted. Such supports should involve an incentive framework that encourages firms to see the value of such activities, and proactively supports them to enter into such activities in a self-funding market-based manner. In some cases, marketing strategies should also target the attraction of particular actor types into a system to address specific weaknesses, e.g. capital availability weaknesses (Anderson et al., 2004; Rosenfeld, 1997; vom Hofe and Chen, 2006).

The five EIFRs are discussed in the following sections, while sample SWOT questions relating to the individual EIFRs are presented in the following tables.

EIFR 1: Knowledge infrastructure, resources and skills

Information/knowledge plays a similar role in modern technology intensive sectors as energy/fuel played in the industrial revolution. As the line between basic and applied research becomes progressively more indistinct, modern industries increasingly rely on PREO-generated knowledge for marketable innovations and economic growth. This means the quality and character of a PC's PREO capabilities, resources, skills, and (sticky) knowledge sets are key elements in the synergy processes that influence a

system's development trajectory, due to the existence of local learning processes, technology transfers and spillover effects supported by geographic and cultural proximity (Wolfe and Gertler, 2007; Malecki, 1997; Anderson et al., 2004; Krafft et al., 2011; Chen at al., 2011; Lundberg and Andresen, 2012).

Cluster specific initiatives must seek to optimise a PC system's knowledge-base by addressing PREO infrastructural weaknesses/gaps, as technological infrastructure limitations restrict innovative activities by limiting research activities. This directly relates to the development of advanced and specialised factors that are necessary for enhancing a system's production capabilities, capacity, and accumulation of technological capabilities (Anderson et al., 2004; DTI, 1999d; MacPherson, 1998; Porter, 1998; Lundberg and Andresen, 2012).

Aside from the importance of a PC's PREO-based research base in innovative and entrepreneurial developments, their education programs play central roles in determining the quality of a region’s skilled labour force. A suitably educated labour base is crucial, as a strong labour pool plays a key role in entrepreneurial and innovative spillovers (Anderson et al.2004; Prevezer and Swann, 1996; Asheim and Isaksen, 2002; Engel and Del-Palacio, 2011; Delerue and Lejeune, 2011).

Initiatives must also focus on the development of suitably skilled labour through training courses tailor-made to the demands of the entire system. Ideally these should be formulated through public/private dialogue as worker skills and attitudes are invisible (tacit) factors in a PC system, in relation to economic diversity and competitiveness (Wolfe and Gertler, 2007; MacPherson, 1998; Engel and Del-Palacio, 2011; Lundberg and Andresen, 2012).

Table 2.8: Sample Knowledge Infrastructure, Resources and Skills SWOT Questions
Is a PC's existing knowledge base analytical and/or scientific in nature? What is the current state of a PC's research infrastructure? Are there important knowledge skill and infrastructure gaps? Are skills of required quality and diversity for all areas of the PC system? Is the whole value chain represented? Is the knowledge base expected to change in the next decade/decades? What infrastructural and skills-related issues may develop as the PC's system develops and evolves? Do PREOs and education providers have the resources and ability to respond to these changes?

Additionally, efforts must be made to support a PC system's ability to retain skilled actors, in particular researchers, and deepen the system's skills base through actor immersion strategies, i.e. short-term placement programmes in other systems so as to

engender the development of more complex skill sets (this directly relates to EIFR 4) (Anderson et al., 2004; Koehler, 1996; Erden and von Krogh, 2011).

EIFR 2: Entrepreneurial infrastructure, resources and skills

High quality PREO assets (EIFR 1) cannot offset the lack of an entrepreneurial or innovative climate in a PC. As stated, vigorous entrepreneurial and innovative activity, and the active participation of entrepreneurs in the building of institutions, aided by forces of agglomeration, are fundamental elements which facilitate the formation and development of a cluster system (Porter, 1998; Romanelli and Feldman, 2007; Scott, 2007; Engel and Del-Palacio, 2011).

A PC's innovative and entrepreneurial propensity is determined by its regional entrepreneurial infrastructure and supports, and the psychological and/or social characteristics of its actors. Entrepreneurship is an endogenous process, a learned set of guidelines that co-evolves with a region's business activities and supports, creating a cluster specific culture. By creating new companies, entrepreneurs spark regional industrial transformations by indirectly building institutions that promote their sectoral needs, thus influencing path dependence and self-organisation (Feldman and Braunerhjelm, 2007; Wolfe and Gertler, 2007; Engel and Del-Palacio, 2011).

Cluster specific policies must focus on the long-term development of a suitable local business environment, and on the inculcation of an entrepreneurial/innovative culture among system actors, to support entrepreneurial/innovative developments and experimentation. Essentially, a multi-faceted support system must be developed, shaped by patterns of public/private interaction and dialogue, which inter-link and co-evolve with a cluster's development so as to facilitate 'organic' system wide developments. Such a support system should focus on 'hard' and 'soft' resources and supports that upgrades the innovation capacity of firms, promotes rapid technological diffusion, and seeks to develop increased interactions between a system's actors (Compete, 2005; Anderson et al., 2004; Malecki, 1997; Lundberg and Andresen, 2012; Eisingerich et al, 2012).

Public supports must be extensions, not replacements, of existing supports, and they must avoid reducing entrepreneurial and innovative pressures in a system. It is also essential that initiatives ultimately seek the development of privately organised supports which are entrepreneurial in nature, so as to respond optimally to a system's evolving nature and needs. This is also important due to their impact on the entrepreneurial character of new

firm developments and of the wider PC system (Feldman and Braunerhjelm, 2007; Scott, 2007; Porter, 1998; Delerue and Lejeune, 2011).

'Hard' system supports include infrastructures and resources that facilitate new, and optimise existing entrepreneurial and innovative developments. These include a suitable legal and regulatory framework and supports, in particular an optimised IP regime, and the availability of a complex range of financial supports and actors. A PC's legal/IP system and skills base must be of suitable quality and of sufficient depth of experience to encourage and protect systemic developments, as weaknesses can deter actors from entering commercial alliances due to the presence of excessive risk levels. Additionally, to develop and maintain entrepreneurial/innovative pressures, sectoral benchmarking should be adopted through the development or application of a suitable regulation system, e.g. the ISO 9001 quality management system (Anderson et al., 2004; Scott, 2007; Wolfe and Gertler, 2007; Maskell and Kebir, 2005; Engel and Del-Palacio, 2011).

A PC with a limited track record of successful entrepreneurial developments will experience cumulative disadvantages in the number and type of investor actors and supports it will develop and/or attract, thus creating a negative feedback loop which undermines entrepreneurial developments. Where one funding source or investment actor type is present/dominant, it limits the type of actors which can access such funding as investor actors, in seeking to optimise their investment returns, have specific requirements and foci to their investment decisions (Romanelli and Feldman, 2007; Owen-Smith and Powell, 2007; Porter, 1998; Graf and Krüger, 2011).

The public/private dialogue can animate the development of a wide range of new financial instruments and supports to facilitate different forms of innovative activities. These include seed and risk capital funding for new high-risk areas, and brokerage services between innovators and the banking sector, including business angels, so as to optimise the business models and the development trajectories of new firms. Public initiatives and supports should be introduced to facilitate the development of new entrepreneurial/innovative firms to build up perceptions of reliability and trust among regional partners in order to attract private investors into the system from other related sectors. Funding and investor variety provides entrepreneurs with viable alternatives and reduces the demand for/over-reliance on existing supports, including an over reliance on public supports (Maskell and Kebir, 2005; Cooke, 2002; Zhang and Haiyang, 2011; Engel and Del-Palacio, 2011; Lundberg

and Andresen, 2012).

Competitive tendering processes should also be introduced in funding initiatives to drive the quality of a PC's entrepreneurial/innovative developments. A realistic 'standard', relevant to the system's state of development, should be adopted, but one which becomes ever higher as the system develops (Owen-Smith and Powell, 2007; Maskell and Kebir, 2005).

However, 'hard' support structure can only assist, and not create innovative/entrepreneurial developments. If the necessary competences and skills required to facilitate entrepreneurial developments do not exist, or are underdeveloped, actors will refrain from such developments due to prohibitive levels of perceived and/or actual risk. Entrepreneurship is an inherently localised phenomenon. Actors typically start companies based on prior experiences and interests. For example, they may seek to address an identifiable niche market existing firms may not acknowledge or find too small or risky to act on, and/or by using existing skill and knowledge sets to develop applications from licensed patents. As such, 'soft' PC system supports must form, advancing existing skills and introducing new skill sets to ultimately create an entrepreneurial culture (Casper, 2007; Orsenigo, 2007; Owen-Smith and Powell, 2007; Krafft et al., 2011; Eisingerich et al, 2012).

In the context of EIFR 1, entrepreneur and researcher skill sets should overlap to optimise value chain developments. This relates to the need for PREOs to develop courses tailor-made to the evolving demands of an entire system. Entrepreneurial/innovative skills can also be engendered through inter-firm/PREO placements, which also facilitate tacit knowledge exchanges. Such programmes are important as entrepreneurial developments are influenced by the pre-entry background of their founders, i.e. preceding tacit knowledge, experiences and contacts from their past working and/or educational activities (Feldman and Braunerhjelm, 2007; Scott, 2007; McKelvey, 1996; Erden and von Krogh, 2011).

Such skills-based initiatives, in alliance with a PC's 'hard' supports, feed the inter-related development of a PC's support ecosystem, and its entrepreneurial/innovative culture. In combination, they facilitate significant long-term cumulative benefits relating to a system's entrepreneurial orientation, which is determined and facilitated by a growing company base. Different forms of entrepreneurial developments can be characterised, as detailed

in Table 2.9.

Table 2.9: Different forms of entrepreneurial developments
Start-up firms: new, relatively inexperienced entrepreneurs seek to develop new commercial developments in a PC. Such firms emerge only when a suitable support framework emerges that lowers entrepreneurial 'entry barriers', through removing/reducing firm development risks, and which also encourage commercially minded actors to abandon their relative job security so as to establish and work within start-ups which have no guarantee of succeeding.
Spin-out firms: new firms form through activity diversification from a related sector. The development of a support framework can 'brand' a PC's innovative capabilities and capacities and attract non-local actors into a PC's system. This also strengthens a PC's capabilities by creating positive externalities, which further lowers entry barriers.
Spin-off firms: new firms can emerge from within a PC system, e.g. actors seek to exploit commercially-viable PREO-based research, or create new ventures that address organisational problems/inertia in their 'parent' actor. Such developments will only occur where a suitable ecosystem is present.

After (Compete, 2005; Casper, 2007; Dahl, Pedersen and Dalum, 2003; Eisingerich et al, 2012).

Spin-off firms are central elements in facilitating positive feedback in a PC's trigger event, as their innovations are likely to be path-breaking in nature, and they open new industrial sub-markets. Additionally, they are more integrated into a PC's internal structures because of the nature of their origin, i.e. their founder(s) have preceding PC-specific research and/or entrepreneurial knowledge and experience. As they would derive their internal structures, routines and practices from existing system actors, they would be perceived as being more trustworthy by a PC's actors in comparison to spin-out and start-up developments. This means they are able to access local entrepreneurial supports and skill sets, improving their probability of success (Dahl, Pedersen and Dalum, 2003; Segenberger and Pyke, 1997; Morgenroth and O'Malley, 2002; Engel and Del-Palacio, 2011; Delerue and Lejeune, 2011).

Table 2.10: Sample Entrepreneurial Resource and Skill SWOT Questions
What skill and service barriers exist that inhibit new entrepreneurial/innovative developments? How advanced and suitable is a PC's IP regime for its current activities? Are professional service firms specialised on the particular needs of the PC? Do PC actors have to access non-local professional service and skill sets? Are a PC's VCs mainly public or private in nature? How diverse are the types/sources of finance available to a PC? Does an observable entrepreneurial/innovative mindframe/culture exist?

Overall, a PC's entrepreneurial support framework sustains and upgrades competitive advantage by facilitating new business model developments through providing the required flexibilities and opportunities to experiment. This framework can also facilitate the development of technological and/or organisational structures which engender different, yet complementary, business activities to a system's 'core' activities. This allows a PC to avoid systemic 'lock-in' developments (Carlsson, 2007; Wolfe and Gertler, 2007; European Commission, 2006; Graf and Krüger, 2011).

EIFR 3: Networks

Clusters are inherently interactive in nature and are characterised by extensive vertical

and horizontal networks. Geographic proximity has little influence beyond providing the appropriate contexts in which an industry can be supported and encouraged to grow, while transfers of knowledge through trust-based interactions/spillovers cannot develop to any level of complexity or depth solely through the use of NICTs. As such, inter-actor networks must form a central aspect of cluster specific policies (Rosenfeld, 1997; Forfás, 2004; Porter, 1998; Carlson, 2007).

An important aspect of competitive clusters is the ability of cluster actors to network extensively *and* to form networks selectively, as rapid exchanges of information/knowledge and externalities (spillovers) from such transfers are pre-requisites to create the necessary synergies that result in a PC's trigger event. This relates to the interactive nature of Porter's diamond determinants (Porter, 1998; Europe Innova, 2008; Anderson et al., 2004; Krafft et al., 2011).

Networks play a central role in the nature and character of the EIFRs, e.g. the development of spatially sticky PREO-based knowledge (EIFR 1) and its exploitation (EIFR 2) through filtered tacit knowledge. Additionally, networks are crucial for developing a cluster's internal logic, with respect to mimetic isomorphism and its impact on network density, and represent a value chain's 'synergy', i.e. the presence of an interactive industrial structure. This synergy cannot be created through top-down initiatives, but must develop through trust-based inter-actor networks. However, significant challenges exist in developing networks, as detailed in Table 2.11.

Stimulating cooperative behaviour in locations lacking a pre-existing collaborative culture is complicated, as the fundamental element of trust in the formation and functioning of networks cannot be created solely through policy. However, networks can form through a mixture of induced and organic processes through a promotion programme which seeds the concept of inter-actor networks and supports their emergence. Multiple examples of such programmes exist internationally, yet the template upon which they are developed is the Danish Government’s Network Cooperation Programme (NCP), launched in 1989. The NCP was sponsored by the Danish Industry Ministry, and sought to improve the international competitiveness of Denmark's then non-networked SME dominated industrial base. The NCP drew inspiration from the 'third Italy' region in the Northeast of Italy, as detailed above (Forfás, 2004; Ffowcs-Williams, 2000; NESC, 1996; Engel and Del-Palacio, 2011).

Through a review of the NCP, and various derivative programmes, two key attributes can be identified. Firstly, network programmes focus on proactive human resource-based promotion activities through a broker programme/service that identifies potential networks and encourages their development. Brokers, optimally, are actors with extensive local knowledge, e.g. a locally-based consultant or economic development agent. Local knowledge is crucial in bringing prospective firms together and establishing information exchange infrastructures, e.g. education and technology support programmes that facilitate interaction and learning synergies, provide advice on the potential benefits of cooperation, and initiate discussions on these benefits amongst firms (Ffowcs-Williams, 2000; Staber, 1996; Martin and Sunley, 2001).

Table 2.11: Issues undermining network developments
Pre-existing levels of cooperation between a PC's stakeholders may be insufficient to organically facilitate network development(s).
A lack of awareness or understanding of the concept and benefits of inter-actor networks may exist among a PC's actors, e.g. networks can be misunderstood as being a quasi-social activity, i.e. 'networking', rather than an important business function, meaning actors would be reluctant to commit time and resources to a process that is not well understood, or whose results are not immediately obvious.
The collaborative aspect of inter-actor networking, i.e. the sharing of resources and knowledge with other firms, particularly competitors, can seem an alien concept to actors that are traditionally protective and secretive.
Actors may rely on a knowledge and information base drawn from their own contacts, meaning they are not in a position to identify the innovative opportunities networks can provide.
Actors may foresee the benefits of inter-actor networks, yet may not have the resources and/or skills required to facilitate or co-ordinate alliances, i.e. a 'collective action problem' can exist.

After (NESC, 1996; Forfás, 2004; Ingley, 1999; Anderson et al., 2004; Kogut, 1988; Lundberg and Andresen, 2012; Krafft et al., 2011).

A broker is also required for transparency, i.e. to engender a pragmatic and uncomplicated programme, as a multi-element programme would require too complex a management structure. Brokers must also facilitate the development of institutional mechanisms relating to formal representation, conflict resolution, and information exchange developments, which in combination, reinforce inter-actor trust and support informal information exchanges (Lagendijk and Charles, 1999; Anderson et al., 2004; Krafft et al., 2011).

The second programme attribute is the provision of financial supports to encourage firms to embrace cooperation. It is important that a suitable support amount should be achieved which is not too generous or too restrictive, and which should diminish over the course of the programme to foster closer inter-actor alliances by avoiding overreliance on, or the exploitation of such funding (Ingley, 1999; Ffowcs-Williams, 2000).

In combination, the hands-on nature of the broker service, and the encouraging nature of

the financial supports address resistance to the programme, e.g. Danish business associations saw cooperation as undermining local entrepreneurship, this was addressed through the programme's hands-on nature (Forfás, 2004; Ffowcs-Williams, 2000).

Following a pilot project to test and optimally fine tune a programme to the specifics of the sector in question, it is run over two principle stages. The first stage involves brokers identifying potential 'networks', which are then 'artificially' induced. This stage involves a consultation phase, introducing both the programme's concept and that of the concept of networks, in alliance with the financial incentives. This approach aims to seed the concept through a learning by doing method, i.e. firms learn about networks through developing their own network dynamics, so as to gain an understanding of the abilities of networks to facilitate or constrain future actions and market opportunities. As such, firms can become more proactive in designing and managing potential future linkages (Gulati, 1998; Ffowcs-Williams, 2000; vom Hofe and Chen, 2006).

The second stage involves creating a favourable institutional setting that encourages firms to explore new forms of business relationships. Essentially, through creating a framework for dialogue and cooperation, in the context of reciprocated investments of time, people and equipment, the second stage seeks to facilitate the evolution of the 'artificially' induced first stage networks into natural, organically developed 'second generation' networks (Ffowcs-Williams, 2000; vom Hofe and Chen, 2006; Forfás, 2004).

Table 2.12: Sample Network SWOT Questions
What is the structure of the PC's value chain? What is the interactive nature of its actors? Are horizontal (informal and inter-actor exchanges) and vertical (formal value chain buyer/supplier relationships) networks present? What is the dominant actor type? Can the PC be characterised as being a 'hub', or 'non-hub' location?

Introducing a network perspective to cluster specific initiatives has important implications for their formulation and implementation. A PC's public and private actors must have a thorough and realistic understanding of the complex dynamics of network formation, the role of facilitation, and the duration and composition of formalised assistance in facilitating behavioural changes, as the trust- and reciprocity-based nature of networks takes time to develop. At minimum, using the NCP as a rough template, a network programme should cover a 3-to-4 year period in order to facilitate the required changes in firm behaviour patterns. These issues again highlight the importance of a

highly responsive and long-term cluster specific policy environment (Ingley, 1999; Forfás, 2004; Ffowcs-Williams, 2000; Malecki, 1997; Larson, 1993).

Additionally, no agreement exists among various academic reviews of network programme case studies as to what constitutes a successful network programme. Depending on the measurement(s) used, dramatic variations in a programme's outcome(s) can be viewed. Indeed, the NCP's evaluation report, the Amphion Report (1996), found that the programme was a failure when it was judged in relation to the longevity of the artificially introduced networks, as the networks which survived developed between actors which had prior close associations and linkages, i.e. inter-actor trust had already been established. However, when firm profitability, market share, and individual firm competitiveness were assessed, the programme was deemed a success. Essentially, the 'co-operation' effect, rapid consultation, interaction and rapid response go beyond what can be measured/accounted for through transmission costs. As such, prior to a programme being run, its 'targets' must be clearly identified, which can be determined through a SWOT analysis (see table 2.12) (Ffowcs-Williams, 2000).

EIFR 4: Market information exchange resources

Technical and structural differentiation among a PC's actors impacts on a system's internal synergy. The development of market information exchange resources, i.e. intermediary institutions and actors, including cross-cluster discussion forums (which may be themed, in relation to a PC's EIFRs), and intermediary technology transfer resources, such as science parks and incubators, can facilitate cross-system information dissemination, mimetic isomorphism, and spillover developments. As such, this EIFR is inherently related to, and indeed facilitates inter-actor network developments (Porter, 1998, Anderson et al., 2004; Delerue and Lejeune, 2011; Forfás, 2004; Simon and Tellier, 2011).

Cross-cluster discussion forums should draw from regional development organisations, government councils, e.g. innovation councils, trade associations, chambers of commerce, and a PC's supplier actors, as they are key conduits for transmitting information between a system's actors. Discussion forums are particularly important in relation to the collection and dissemination of information on a system's technology, skills, and management- and market-related developments. Such services are important as all actors cannot be fully up-to-date with or access all the relevant information on a system's developments, e.g. new technological and market segment developments, due

to their limited resources (Daskalakis and Kauffeld-Monz, 2007; Oughton et al., 2002; Delerue and Lejeune, 2011; Simon and Tellier, 2011)

Discussion forums can also inform a PC's public/private dialogue process, and can expedite the development of a support ecosystem by identifying specific skills and competence weaknesses. Discussion forums can also impact on the visibility of a PC's 'brand', regionally and internationally, through optimising a system's support ecosystem and entrepreneurial/innovative activities. This can facilitate the development of pro-active initiatives to access and exploit non-local skills, competences and resources. Cross-PC/cluster discussion forums can identify common issues among different systems, cross-pollinate skills and competences to stimulate entrepreneurial and innovative developments, and encourage diversification that prevents systemic 'lock-in'. Additionally, short-term actor placements in more endowed PCs and/or fully developed systems can also seed non-local skills and competences in a system (Scott, 2007; Martin and Sunley, 2001; vom Hofe and Chen, 2006; Morris, 2011; Graf and Krüger, 2011).

Discussion forums can also facilitate entrepreneurial/innovative developments through influencing the structures and development of intermediary technology transfer institutions. Two key types can be identified, science parks (detailed further in the following chapter) which act as sectoral research engines through having a specific sectoral focus, and incubators, which facilitate knowledge-based entrepreneurial developments. Both forms are key information exchange nodes between PREOs and industry actors as they typically locate in close vicinity of one, or several PREOs, and facilitate researcher/entrepreneur interactions through transfers of knowledge/information. As such, they allow PREO actors access up-to-date information on the requirements of commercial actors, allowing them to tailor their research programmes towards commercial areas, and they also allow commercial actors access the significant tacit knowledge reserves of PREO actors, and more optimally identify commerciable research, facilitating new entrepreneurial developments (Feldman and Braunerhjelm, 2007; Owen-Smith and Powell, 2007; Scott, 2007).

Table 2.13: Sample Market Information Exchange SWOT Questions
To what extent is the PC's system supported through defined, pro-active information services? Are all actors in a PC's value chain represented in these services? Are there common skills, competences and resource weakness? Have cross-PC/cluster skills and competence exchange initiatives developed? Are technology transfer intermediary institutions present in the system? What skills, competences and/or resources are present in these institutions? How inter-linked are they in relation to on-going PC developments?

Optimally, technology transfer actors should provide a range of hard and soft supports for all stages of commercial developments, i.e. by allowing entrepreneurs/innovators develop market-ready innovations and/or spin-off firm developments. Such supports could include office and laboratory space, equipment and materials, as well as project feasibility studies, market research services, and the provision of business management resources (this feeds into EIFR 2). Discussion forums can feed into the optimal development and implementation of these supports by constant up-dating and tailoring their development through information exchanges on a PC's development trends (Anderson et al., 2004; Forfás, 2004; Malecki, 1997; Engel and Del-Palacio, 2011).

EIFR 5: Actor and institutional density, and skill, competence and resource depth

A PC's trigger event is determined by its system being subject to a structured and self-reinforcing process of growth and development. Such processes are facilitated by the formation of a diverse range of market and non-market actors and institutions, skills, and resources. This depth and density forms due to the EIFRs addressing systemic weaknesses by engendering an adaptive and responsive ecosystem in relation to a system's skills, resources, and institutional structures. This allows a PC to optimise its positive development trajectory, facilitating further EIFR-related developments, i.e. positive feedback inputs occur throughout the PC system, facilitating the development of the four determinants of competitive advantage (Porter, 1998; Keeble et al, 1999; Maskell and Kebir, 2005; Wolfe and Gertler, 2007; Krafft et al., 2011).

Actor and institutional density is important in setting the overall context or framework in which clusters develop. It represents the stratification of a system's functions, i.e. the development of vertical and horizontal networks, facilitated by cross PC market information exchange resources. Skill and resource depth facilitates interactive synergies that a cluster system and its determinants require. These synergies, which include a PC's social structure, can be considered system-specific support structures that reinforce its competitive advantage, i.e. actor attitudes, practices, and connections become a key part of a region’s non-replicable asset base by influencing future actor behaviour through mimetic isomorphism (Maskell and Kebir, 2005; Wolfe and Gertler, 2007; Gilding, 2008; Zhang and Haiyang, 2011; Howells and Edler, 2011)

Where a PC fails to organically develop actor and institution density and depth, it experiences difficulties in developing agglomerated economies, and other critical mass opportunities. Failure to develop density can occur due to limitations in a PC's

population and/or market size, which can prevent user-producer interactions, restrict information flows, and prevent the formation of a sufficient base of related and interlinked firms. These issues restrict a system's ability to develop skill and resource depth, meaning it is unable to keep up with and/or exploit technological and innovative developments due to limited information exchanges (Malecki, 1997; Wolfe and Gertler, 2007; Krafft et al., 2011; Howells and Edler, 2011).

To address these issues, an 'anchor' actor strategy can be developed to facilitate positive externalities throughout the PC system, and to drive systemic depth and density by engendering coordinated networks of interconnected actors. There are three anchor firm strategy models.

The first model is that of a PC's system organising around the organic development of a 'star' actor, e.g. a trail blazing firm which experiences significant first mover advantage, or through chance/indirect developments, e.g. organisational problems/inertia in an existing actor resulting in new spin-off developments. Such developments may form due to serendipitous events, e.g. the chance development of a novel technology, direct policy interventions, e.g. investments in research facilities resulting in technological advances, and the development of a coordinating organisation/body which acts as a manager for the system's development. Such developments can boost a PC's system by signalling underexploited/latent systemic strengths and opportunities to the wider PC system, thereby encouraging actors to seek further innovative and entrepreneurial developments, thus facilitating significant positive feedback inputs (Dahl, Pedersen and Dalum, 2003; Kaiser, 2002; Porter, 1998).

The second model is that of a PC's system organising around the facilities of TNCs, i.e. local TNC or FDI branch plants. Lazerman and Lorenzoni (1999) note that while clustering typically involves SMEs, TNCs can make important contributions to local economic development in many different ways. Where TNCs are embedded in a system, they can facilitate positive externalities, such as integrating scientific and management competences into the system, which can result in technological advances and new start-up developments. To attract TNC interest, a PC must have globally recognised PREOs that focus on TNC-related research areas and/or firms engaged in relevant technological areas with IP suitable for R&D investment. By virtue of their size, TNCs can facilitate access to global markets, facilitate significant skills exchanges with non-local

PCs/clusters, and prevent/address regional insularity (Anderson et al., 2004; Birkinshaw, 2000; Enright, 2000; Porter, 1998; Lee, 2012; Eisingerich et al, 2012).

Alternatively, TNC FDI activities can be introduced, in what Enright (2000) calls a 'transplant' strategy, to address weaknesses in a PC's system. FDI developments can provide significant systemic inputs due to the construction of TNC facilities and supporting infrastructures, the provision of financial supports as part of their inward investments, the attraction of non-local service providers to a region, and can also provide local actors with access to alternative finance sources through collaborative partnerships (Anderson et al., 2004; Birkinshaw, 2000; Malecki, 1997; Howells and Edler, 2011; Eisingerich et al, 2012).

The final model is an interdependent model, i.e. a mutually beneficial scenario where a PC and a TNC play interdependent roles in each other's development strategies. In this scenario, FDI can be positive where branch plants seek to become more innovative by forming collaborative alliances with a PC system to access its resources and competences. This can allow a PC's actors to access non-local networks, resulting in the strategic development of new market networks and innovative capacity in the home market. Integrated TNC elements in a PC system advertises the system's ability to successfully develop products and processes, which improves its global profile/brand, which can lead to cumulative positive feedback processes emerging that drive a system's development trajectory (Europe Innova, 2008; Porter & Stern, 2001; Eisingerich et al, 2012).

In relation to the second and third models, Casper and Murray (2005) comment that the strength of a PC's ecosystem is important in how it adapts to and addresses the institutional characteristics of TNCs. TNCs will proactively work within an ecosystem that facilitates significant entrepreneurial and innovative developments, thus creating significant positive feedback inputs. Yet, TNCs can facilitate negative inputs in several ways. Their presence in a poorly developed PC can drain off important local skills and resources due to their more asset rich nature, relative to local PC actors. Additionally, TNCs have "little experience in memory of entrepreneurial activity" (Romanelli and Feldman, 2007: 109) due to their age, meaning they can undermine the formation of an entrepreneurial culture, while their size and vertically structured nature can inhibit the dissemination of information on entrepreneurial and innovative developments, undermining network and spillover

developments (Casper and Murray, 2005; Porter, 1998; Anderson et al., 2004; Biggerio, 2002).

Casper and Murray (2005) also comment there are several issues with FDI 'transplant' strategies. The degree of embeddedness of TNC FDI operations in a system depends on the level of autonomy they have from their parent operations, which is dependent on how technology intensive their activities are. Branch plant investments can be unstable due to their sensitivity to cost changes and to regulatory changes in the TNC's home nation. If a PC system relies on FDI activities, it may fail if such an actor leaves the system. Additionally, where FDI is introduced without a defined regional emphasis and/or logic, i.e. branch plants are placed in locations due to political pressures, not as aspects of a regional development strategy, it can result in the development of 'cathedrals in the desert', i.e. branch plants located in areas where they cannot link into the local economy due to limited actor numbers and activity levels (Porter, 1998; Brown, 2000; Graf and Krüger, 2011; Eisingerich et al, 2012).

Table 2.14: Sample Actor Thickness and Institutional Depth and Density SWOT Questions
What is the scale of the PC in relation to its geographic, population and market size? Are aspects of the PC's scale expected to change? What is the scale, scope and character of a PC's ecosystem? What is the state and scale of a PC's firm base? How developed are a PC's business management competencies, including the presence of experienced non-executive directors in a cluster? What is the state and scale of dedicated service providers, professionals and technical actors? What is the scale, scope, character and degree of integration of TNC operations presence in a PC system?

These issues mean that 'anchor' strategies must be developed through the public/private dialogue in order to evaluate their suitability to a PC system, and to optimise the degree of embeddedness of TNC operations (Porter, 2000; Anderson et al., 2004; Rosenfeld, 2002).

2.4.6 Cluster informed policy themes

Where a cluster emerges, subsequent policies will be cluster informed in nature. Such policies are less comprehensive than cluster specific initiatives due to the presence of an established support ecosystem that acts like a collective entrepreneur. No formal cluster mapping exercise is required or undertaken, as only specific system aspects are examined. As cluster informed policies are system specific and unique to a specific point in a cluster's development trajectory, general themes cannot be detailed/caricatured. However, in the context of the cluster emergence and development themes, clusters require sophisticated enabling actions and practices which concentrate of advancing the development of a cluster's entrepreneurial and innovative environment.

As such, where interventions are required, they will focus on systemic adjustments, responding to emerging needs/requirements to optimise a system's performance (Wolfe and Gertler, 2007; Anderson et al., 2004; Malecki, 1997).

Cluster informed initiatives should also seek to optimise second generation firm developments, and to attract non-local actors into a cluster system so as to extend and consolidate its competitive advantage(s). There are two key non-local actor types whose presence indicates a system's maturity level, non-local TNCs and entrepreneurial support actors, in particular VCs. The presence of TNCs demonstrates the presence of suitable research activities and commercial developments, while non-local supports indicates the presence of a highly entrepreneurial environment. Their presence facilitates the further advancement of a highly advanced and complex entrepreneurial support ecosystem (Orsenigo, 2007; Feldman and Braunerhjelm, 2007; Anderson et al, 2004; Graf and Krüger, 2011; Kolympirisa et al., 2011).

2.5 CONCLUSION

This chapter lays the theoretical foundation from which the remainder of the thesis is constructed.

It demonstrates that the flexible forms of production associated with Post-Fordism are based on self-organised trust- and reciprocity-based inter-actor networks. Networks facilitate innovative development by addressing the bounded rationality of individual actors through the more optimal use and combination of various types of resources and exchanges of filtered knowledge. Such exchanges are optimised where close relationships have formed between actors that are located in close geographic proximity to each other (Zhang and Haiyang, 2011).

The chapter demonstrates that geographic variations in regional endowments of firms, institutions, and social capital mean that non-reproducible regional specific organisational forms and targets emerge that link together to form a local knowledge community, or organisational field, which determines the innovative capabilities and development trajectory of sectoral actors (Engel and Del-Palacio, 2011; Graf and Krüger, 2011; Huggins et al., 2012).

Where dense agglomerations and critical masses of actors, resources, infrastructures and networks emerge, industrial clusters may develop. Clusters represent more organised and

co-ordinated territorial systems which can be characterised as being intensely entrepreneurial and innovative in nature, and whose internal functions stratify organically, i.e. vertical and horizontal networks emerge through private actor developments (Krafft et al., 2011).

The chapter demonstrates that the reasons why particular locations develop clusters, and others not, are reflected in the diverse and place specific elements of a nation, i.e. its resources and place specific historical traditions and cultures. Clusters are born and develop on the basis of case specific combinations of capabilities, incentives, and opportunities. Their development occurs when an area's favourable pre-conditions, e.g. naturally occurring factor conditions and/or seeds (directly or indirectly introduced positive elements), facilitate the emergence of a proto-cluster system in the context of a system specific trigger process that is determined by its development trajectory. Clusters emerge as a result of a trigger event, i.e. the development of critical masses of actors, entrepreneurship, resources and skills. Such events are system specific, and can occur through either spontaneous, planned or hybrid processes. Emerging clusters become self-reinforcing and self-sustaining through attracting key non-local actors into the emerging cluster system, and the development of second generation entrepreneurial developments.

Where Governments seek to facilitate cluster emergence, they must seek to engage with existing competences and pre-conditions/seeds, and tailor policy initiatives to the particular circumstances of the sector in question. The chapter demonstrates that a system specific multi-faceted support ecosystem based around the inter-linked EIFRs should be developed through a continuous public/private dialogue process that introduces key infrastructures and supports to engender private actor entrepreneurial and innovative developments which facilitate a cluster's trigger event.

Where clusters emerge, governance structures will be mainly private actor dominated, supported by public actor measures that seek to fine tune the regulatory environment within which a cluster system is based. Such measures seek to support the entrepreneurial environment of a cluster system, to optimise second generation firm developments and the attraction of key non-local actors.

CHAPTER 3:
THE ORGANISATIONAL STRUCTURES OF THE INTERNATIONAL BIOTECHNOLOGY INDUSTRY

3.1 INTRODUCTION

This chapter details the organisational structure of the international biotechnology sector (bio-sector), and draws from the theoretical descriptions of inter-actor networks and industrial clusters presented in the previous chapter.

The international bio-sector's structure is an example of the network absorption capacity of small high-tech Post-Fordist firms, in which small biotechnology firms (bio-firms) co-exist and interact with established Transnational Corporations (TNCs) and other sector actors in a variety of alliances/collaborations with different partners at different stages of the product development process (Giesecke, 2000; Harrison, 1997).

Networks are not solely at the heart of the development of the international bio-sector, as the networks that characterise it emerged from distinct geographic roots. Many of the organisations that forged the bio-sector’s complex relationships are located in close geographic proximity to each other, meaning these networks are spatially concentrated in what are identified as industrial clusters (Visser and Boschma, 2002; Romanelli and Feldman, 2007; Feldman and Braunerhjelm, 2007).

The first section draws from the theoretical description of industrial clusters, as presented in the previous chapter, and examines the development of biotechnology clusters and proto bio-clusters in the international bio-sector. This is derived through the analysis of key international bio-sectors. The second section draws from the theoretical descriptions of the motivations and characteristics of inter-actor networks, as presented in the previous chapter, to present typologies of the key sectoral actors and formal and informal inter-actor networks that are found throughout the complex, multi-stage, semi-sequential biotechnology innovation/drug development process. This section also details regional differences in bio-sector network structures. The third section presents a bio-cluster development policy template, based upon the entrepreneurial and innovative functional resource template presented in chapter 2, and observed patterns and themes in international bio-clusters. This identifies the main themes required to facilitate positive systemic feedback inputs and to optimally drive a proto bio-clusters' development trajectory in order to expedite a bio-cluster's emergence and sustainable development.

3.2 CLUSTERS IN THE INTERNATIONAL BIOTECHNOLOGY INDUSTRY

Regional endowments of actors, their institutional and non-institutional characteristics, and how regional specific organisational forms developed, mean that hub and non-hub biotechnology sectors (bio-sectors) can be identified in the international sector (Malecki, 1997; Owen-Smith and Powell, 2007; Huggins et al., 2012).

The 'hub' bio-sectors form dense geographic concentrations of actors, whose network structures are spatially concentrated in what are identified as industrial clusters, i.e. inter-actor networks "played an essential role in the development of stable regional clusters...[but clusters have] seeded the geographically dispersed structures that have come to characterize" (Owen-Smith and Powell, 2007: 63) the international bio-sector's hubs (Breschi et al., 2001; Giesecke, 2000; Prevezer and Swann, 1996; Anderson et al., 2004).

Few locations have developed biotechnology clusters (bio-clusters) internationally. Three US-based bio-clusters can be observed, i.e. San Francisco, Boston and San Diego, while only two non-US bio-clusters can be identified in Cambridge and Munich. Outside of these bio-clusters, 'non-hubs' are essentially little more than agglomerations of co-locating actors, principally biotechnology firms (bio-firms) and Public Research and Education Organisations (PREOs), grounded in regional ambitions to become significant players in the global sector. They exhibit and/or mimic structures and practices found within bio-clusters, yet fail to develop defining aspects, characteristics and features of bio-clusters due to place specific reasons, e.g. regional limitations in the numbers and types of institutions, resources and specialist suppliers. These locations can be termed proto bio-clusters (PBCs) (Wolfe and Gertler, 2007; Delerue and Lejeune, 2011; Powell et al., 2002; Gertler and Levitte, 2005; Malecki, 1997; Graf and Krüger, 2011).

The following sections draw upon the cluster development trigger process and event themes presented in chapter 2, and detail the observable patterns in the different bio-clusters and PBCs, drawing extensively from international case studies, so as to identify common features in the development and structures of the international bio-clusters, and common features in the development and structures of a selected number of PBC case studies, including common issues which undermine their development trajectories and trigger processes.

3.2.1 Bio-cluster development themes

General similarities can be identified in the factors which facilitated the emergence of the observable bio-clusters systems, i.e. similar positive pre-conditions and seeds can be identified, while similarities can also be identified in their internal network structures. In part, these commonalities are due to Genentech's foundation in 1976 establishing both the international bio-firm development template, and the form/character of the bio-sector's innovation process/value chain.

Despite such similarities, the individual bio-clusters emerged due to case specific trigger processes which built upon and primed their case specific pre-conditions and seeds, engendering the formation of entrepreneurial and innovative support ecosystems tailored to the specific demands and requirements of their emerging cluster systems, and ultimately facilitated a system-specific trigger event through the development of a critical mass of entrepreneurial and innovative activity.

3.2.1.1 General development themes of the US bio-clusters

The US bio-sector emerged in the context of significant Federal- and State-level preconditions and seeds that directly and/or indirectly related to biotechnology. These preconditions/seeds developed due to direct and indirect impacts of the significant advanced and specialised Federal Cold War factor investments in the country's Public Research and Education Organisation (PREO) infrastructures and research programmes. These investments linked in with existing Federal structures and organisations, in particular the National Institutes of Health (NIH), the main US health and biomedical research agency which was established in 1930. As such, the US had developed a substantial PREO infrastructure with an advanced resource and research skills base, by the 1970s (Marrs, 2001; Giesecke, 2000: Romanelli and Feldman, 2007; Erden and von Krogh, 2011)

From the mid-1950s onwards, the Federal Government sought to exploit the significant commercial potential resulting from the Cold War PREO funding initiatives, and introduced advanced commercially orientated structures to the PREOs. Additionally, to engender a suitable commercialisation support environment, the Federal Government introduced the Federal Small Business Administration (1953) to assist the development of an innovative SME base**,** and the Small Business Investment Act (1958) to facilitate the proliferation of private speculative investors. The Small Business Investment Act linked in with the then emerging private US Venture Capital (VC) industry (Barry,

2007; Cooke, 2002).

It is important to note that these support structures sought to facilitate developments in the wider economy, not just in one sector, and represented the coordination of Federal Government innovation and industrial policy threads/strands. This is an on-going process, as detailed further below (Casper, 2007; Owen-Smith and Powell, 2007).

In combination, these developments initiated a long tradition of indirect Federal supports to facilitate and optimise SMEs/high-tech firm developments from PREO-based research, and inculcated an entrepreneurial mindframe/culture among the US PREOs due to the substantial commercial rewards conveyed through successful commercial developments. Other significant preconditions/seeds that facilitated the US bio-sector's emergence included the established nature of the US pharmaceutical sector, the presence of a wealthy private actor-driven health-care system, which drove Transnational Corporation (TNC) R&D activities, and the New York-based NASDAQ stock market. This was established in 1971, and played a crucial role in the US bio-sector's subsequent development (Casper, 2007; Owen-Smith and Powell, 2007; Cooke, 2002).

- **The San Francisco bio-cluster's trigger process and trigger event themes**

The San Francisco bio-sector emerged following Genentech's foundation in 1976. The nature of Genentech's formation and development, detailed in chapter 1, characterised/symbolised the Bay Area's preconditions and seeds. These included:

- the absence of 'traditional' disciplinary department structures in the area's PREOs. Their interdisciplinary and cross-functional organisational models were derived from those of the National Institutes of Health;
- the presence of an advanced, commercially orientated PREO base, whose biotechnology-related research programmes were (and remain) focused on translating basic science into clinical applications due to the focus of the various Federal Government programmes on facilitating PREO-based commercial developments, and;
- San Francisco's close proximity to the highly evolved and innovative high-tech support ecosystem of Silicon Valley (SV) (Owen-Smith and Powell, 2007; Feldman and Braunerhjelm, 2007; Delerue and Lejeune, 2011).

SV impacted on the bio-sector's development trajectory in numerous ways. The area's

fledgling bio-firms tapped into SV's pre-existing structures, e.g. SV's advanced financial and business management development services and communications networks, and adopted SV's pre-existing business structures and cultures, including its high labour mobility structures and entrepreneurial mindframe. Essentially, SV's established entrepreneurial climate and evolving support structures acted as a model for the Bay Area bio-sector, which increased the Bay Area actors' ability to access SV's resources through mimetic isomorphism (Powell et al. 2002; Prevezer and Swann, 1996; Europa, 2003; Delerue and Lejeune, 2011).

These features linked into the defined entrepreneurial culture and open organisational structures bio-firms derived from the department organisations of their 'parent' PREOs. The PREOs had a preference for "informal, non-contractual ties in their regional networks [which] enabled financiers to shape innovation and organisational strategies" (Owen-Smith and Powell, 2007: 81). The open organisational structures facilitated rapid information diffusion, i.e. substantial spillovers occurred, and the system's bio-firms formed overtly commercial approaches in the typical products they developed and in the alliances they formed (Powell et al. 2002; Prevezer and Swann, 1996; Feldman and Braunerhjelm, 2007).

A key element in the structural development of the bio-sector was SV's experience in dealing with, and supporting the development of high-risk high-technology electronics and new information and communication technologies (NICT) firms, i.e. SV's VC firms understood the crucial nature of tacit and codified knowledge exchanges, through informal and formal inter-actor networks, in their development. Additionally, the VCs understood the level of hands-on financial and business support needed to successfully achieve their desired exit strategy. This innate knowledge significantly impacted on the development of the bio-sector's tripartite value chain, and facilitated the emergence of the San Francisco system's spatially agglomerated nature (Giesecke, 2000; Kenney and Patton, 2007; Chen at al., 2011; Erden and von Krogh, 2011).

Genentech's meteoric development trajectory established its position as the system's anchor actor, and highlighted the significant commercial potential of biotechnology and the depth of the Bay Area's support ecosystem internationally. This resulted in a subsequent surge in bio-firm developments as a 'gold rush' mentality developed as investors rushed to replicate Genentech's successes. Essentially, a 'brand' effect emerged that cemented San Francisco's position at the vanguard of the international bio-sector's development. This

facilitated a positive systemic development trajectory by encouraging commercially minded PREO academics to enter into commercial developments and/or to abandon their relative job security to work within a failure prone start-up bio-firm. Genentech's success also attracted in substantial non-local actor interest from less resource endowed areas, creating substantial spillovers and positive systemic feedback events (Compete, 2005; Casper, 2007; Engel and Del-Palacio, 2011; Graf and Krüger, 2011).

The bio-sector's positive development trajectory was further amplified by the Federal Government optimising the Federal regulatory environment supporting the commercialisation of PREO-based research through introducing the Bayh-Dole and the Stevenson–Wydler Technology Innovation Acts in 1980 (European Commission Research, 2007; InfoService Biotechnology, 2004).

VCs quickly became the dominant actor in the bio-sector's network structure, as in seeking to replicate Genentech's successes, they sought to optimise their investment returns by avoiding the dilution of IP through multiple inter-actor alliances, i.e. limited inter-firm research and/or product development alliances formed between first generation bio-firms due to VCs seeking to engender alliances with TNCs. This development established the system's product commercialisation orientated character. However, due to the rapid proliferation of bio-firms, TNCs could be selective in entering such alliances. As the system's advanced support ecosystem supported entrepreneurial experimentation, the bio-sector responded to this development through engendering second generation firm developments to allow the exploitation of increasingly niche market opportunities (Giesecke, 2000; Chen at al., 2011; Eisingerich et al, 2012).

In the context of the Bay Area's significant preconditions/seeds, its rapid development trajectory, and its advanced support ecosystem, the bio-sector rapidly developed a mass of entrepreneurial and innovative activity and experienced a spontaneous trigger event in the early 1990s. A self-sustaining cluster system rapidly developed as its advanced nature acted as a national and international 'magnet' that attracted non-local actors, skills, competences and resources, particularly non-local TNCs and VCs from outside of SV. These inputs engendered substantial feedback inputs which created a self-sustaining cluster system (Graf and Krüger, 2011; Eisingerich et al, 2012).

The bio-cluster is presently characterised by a dense complex inter-actor network structure,

due to its support ecosystem facilitating and driving niche market exploitation and enabling extensive career mobility between actor types, in combination with the deepening impact of mimetic isomorphism. The ecosystem continues to actively support entrepreneurial experimentation, which has allowed the cluster to avoid 'lock-in' developments, and which allowed the system to restructure itself in the context of the significant VC fluctuations caused by the Dot.com bubble in the 1990s (Owen-Smith and Powell, 2007; Graf and Krüger, 2011).

- **The Boston bio-cluster's trigger process and trigger event themes**

The Boston bio-sector's preconditions/seeds resembled those of San Francisco, i.e. there was an established and commercially orientated PREO base, including the Massachusetts Institute of Technology (MIT) and Harvard University, as well as a significant military research presence due to Cold War era Federal funding. A defined entrepreneurial climate had also formed as PREO derived commercial developments and advanced support structures had facilitated the development of a major electronics agglomeration by the mid-1970s (Judge, 1997).

The bio-sector's trigger process emerged spontaneously following Genentech's emergence, yet its development trajectory took a different form than the Bay Area's trajectory due to the unique institutional characteristics of its actors.

While SV's VCs facilitated and drove the San Francisco bio-sector's rapid development, VC involvement in the Boston bio-sector's development was relatively minor as few local VCs existed due to the area's proximity to New York. The bio-sector emerged and developed in the context of the intense commercial rivalry between MIT and Harvard, and the established entrepreneurial supports that had formed around its electronics/NICT agglomeration, i.e. PREOs were the network structure's dominant actor (Owen-Smith and Powell, 2007; Kenny and Patton, 2007; Graf and Krüger, 2011).

In comparison to their San Francisco-based counterparts, Boston PREOs were (and remain) more focused on basic research activities, and were/are more conservatively and rigidly structured. These characteristics were reflected in the bio-sector's structure. PREOs transferred IP to spin-off bio-firms through formal licensing arrangements, which resulted in the bio-firms locating in close proximity to their 'parent' PREO(s). This facilitated the development of a dense PREO-orientated sectoral network structure (Owen-Smith and Powell, 2007; Kenny and Patton, 2007).

Several interlinked elements facilitated the bio-sector's positive development trajectory. The financial success of the bio-sector's first generation bio-firms engendered positive systemic inputs, e.g. the system's anchor actor, Genzyme, was established in 1981 and achieved a successful IPO in 1986. This created a more pronounced commercial mind-set among the bio-sector's PREOs and drove commercial developments throughout the bio-sector which engendered a system 'brand'. This is demonstrated by the entry of the manufacturing facilities of Geneva-based Biogen, which was co-established by an MIT scientist, into Boston in 1983 (Owen-Smith and Powell, 2007; Feldman and Braunerhjelm, 2007).

The bio-sector's development trajectory indirectly benefited from the decline of the area's electronics agglomeration during the 1980s, as the Boston area's minicomputer orientated electronics sector was supplanted by SV's microprocessor innovations, and also through alterations to the Federal Government's research procurement and military funding initiatives in the mid-1980s. Both events released researchers into the system, while the support structures surrounding the electronics agglomeration and the military research institutes (RIs) switched towards other high-tech sectors, including the local bio-sector, feeding into the system's support ecosystem (Watkins, 2004; Engel and Del-Palacio, 2011).

Boston's bio-cluster emerged in the mid-1990s due to a spontaneous trigger event caused by a critical mass of entrepreneurial and innovative activity. A self-sustaining bio-cluster system rapidly formed due to an influx of non-local VCs and TNCs, while the bio-sector's established entrepreneurial environment facilitated the development of second generation spin-off developments by the late 1990s. The system's evolving brand has attracted in significant national and international skills, competences and resources further driving its development trajectory (Owen-Smith and Powell, 2007; Graf and Krüger, 2011; Eisingerich et al, 2012).

- **The San Diego bio-cluster's trigger process and trigger event themes**

Despite the presence of similar preconditions/seeds to those found in the San Francisco bio-cluster, e.g. similar PREO structures and a similar proximity to SV, the San Diego bio-cluster emerged through a very different trigger process and trigger event.

As with the Boston bio-sector, San Diego's bio-sector emerged following Genentech's

establishment. Despite the bio-sector's proximity to San Francisco, its trigger process was initially undermined by two inter-related systemic issues. Up until the mid-1980s, the area's PREO base was dominated by a significant US Army, Air Force and Navy presence which had developed at the beginning of the twentieth century, and then expanded through decades of Federal Cold War funding. As such, the area's PREOs and support structures had a less pronounced commercial orientation due to their focus on a closed dominant actor type (Romanelli and Feldman, 2007; Europa, 2003; Chiaroni, and Chiesa, 2006; Graf and Krüger, 2011; Eisingerich et al, 2012).

By the mid-1980s, limited commercial developments had occurred due to an absence of VC involvement. Only 10 bio-firms had formed by 1986, mainly due to the magnetism of the San Francisco system's brand drawing potential resources away from the San Diego area. San Francisco's magnetism can be demonstrated by the fact that the 1980 changes to the Federal regulations had virtually no direct/immediate impact on the San Diego system at the time. Additionally, and paradoxically, the limited level of commercial activity in the San Diego area undermined the development of a system brand (Romanelli and Feldman, 2007; Europa, 2003; Chiaroni, and Chiesa, 2006).

The system's trigger process experienced two significant and serendipitous feedback inputs which dramatically altered its development trajectory in the mid-1980s. The gold rush mentality which developed after Genentech's IPO in 1980 resulted in the creation of many commercial ventures in efforts to engender Genentech-style results. In 1986, US TNC Eli Lilly bought Hybridtech, a spin-off bio-firm from the University of California, San Diego. As in San Francisco, San Diego's bio-firms adopted the open structures of the local PREOs. This created a clash of corporate management practices between the vertical Fordist structures of the TNC, and the horizontal structured Post-Fordist bio-firm. This led to the majority of Hybridtech's management and research teams leaving the bio-firm (Timmerman, 2010; Chiaroni, and Chiesa, 2006).

Indirectly, Hybridtech became the system's anchor actor and established its internal structure, as a mass of bio-firms were established through money generated from the Hybridtech merger. Indeed, the takeover's fallout ultimately resulted in the formations of nearly 50 first and second generation spin-off bio-firms, while several local VCs were formed by former Hybridtech employees (Chiaroni, and Chiesa, 2006; Casper, 2007).

This development coincided with the Federal Government's expenditure reductions in the mid-1980s impacting on military research expenditure, which indirectly and unintentionally shifted the focus/orientation of the region's military-orientated research and support structure towards the emerging bio-sector. Combined, these serendipitous developments created a surge in commercial activity, engendered a positive systemic development trajectory through facilitating significant systemic feedback inputs, and resulted in the rapid development of a critical mass of entrepreneurial and innovative activity which led to a hybrid trigger event in the mid-1990s (Casper, 2007).

San Diego become a self-sustaining bio-cluster through establishing a complex support ecosystem, including significant local VC developments, that formed a distinct cluster brand which, despite its proximity to the San Francisco bio-cluster, has attracted national and international competences and resources into the system, including TNC R&D facilities. The extensive bio-firm base means a thick level of management and bio-firm development-related expertise has formed, facilitating and driving commercial developments throughout the system (San Diego Workforce Partnership Inc., 2000, 2002; Business Wire, 2004; Casper, 2007).

3.2.1.2 General development themes of the European Union-based bio-clusters

- **The Cambridge bio-cluster's trigger process and trigger event themes**

The Cambridge bio-cluster emerged in the context of similar preconditions and seeds to those found in the US bio-clusters. Cambridge had an advanced PREO base which includes some of the oldest universities in the world, and which have been responsible for many of the technological breakthroughs that facilitated the bio-sector's emergence, including the discovery of the structure of DNA. Additionally, the Cambridge area had developed an electronics/NICTs agglomeration, termed 'Silicon Fen', while a number of pharmaceutical TNC branch plants were also located in the area (Breschi et al., 2001; Chiaroni and Chiesa, 2006; DTI, 1999).

These developments had occurred due to proactive open market initiatives by the UK Government, starting in the late 1960s, to seed non-local skills and competences, e.g. encouraging foreign pharma-TNCs to establish UK operations, and to engender a more industrially proactive orientation in the area's PREOs through developing intermediary actors, such as the Cambridge Science Park, which opened in 1970, that sought to attract NICT companies into the area. These initiatives and supports facilitated the emergence of localised high-tech service infrastructures and an evolving public and

private commercialisation support environment (Simpson, 2002; Chiaroni and Chiesa, 2006; DTI, 1999; Cooke, 2002; Graf and Krüger, 2011).

The Cambridge bio-sector emerged in the late 1970s following Genentech's emergence, slotting into the area's evolving entrepreneurial supports. By the late 1980s, the bio-sector had begun developing a mass of entrepreneurial/innovative activity, yet its trigger process was undermined by an absence of key sectoral actors, e.g. initial sectoral developments occurred in a near absence of VC coverage, which was partly caused by the absence of a successful anchor bio-firm. Furthermore, few defined or direct public development initiatives/supports existed. As such, limited feedback developments occurred to drive the bio-sector's development trajectory (DTI, 1999; Cooke, 2002).

The Cambridge system experienced a hybrid trigger event during the mid-1990s through the introduction of a series of UK Government initiatives which developed in response to European Union-wide efforts in the early 1990s to address the increasing global dominance of the US bio-sector. These initiatives focused on supporting the commercialisation of PREO research and engendering PREO/firm networks through the development of major biotechnology-related RIs and intermediary actors, particularly incubator and science park developments, as well as the introduction of dedicated technical and business service providers. Rapid sectoral developments followed which built on the area's existing agglomerated strengths, meaning that Cambridge quickly developed into a self-sustaining bio-cluster system (Casper and Karamanos, 2002; Casper and Murray, 2005).

The bio-cluster system rapidly developed an advanced support ecosystem which facilitated the bio-cluster's progress through a gradual contraction phase in the late 1990s caused by limitations with VC funding due to the Dot.com bubble collapse. Additionally, a system brand has formed which has attracted in national and international skills, competences and resources, including bio-firms originating from non-local PREOs, as well as considerable pharma-TNC activity (Parc Cientific Barcelona, 2010).

- **The Munich bio-cluster's trigger process and trigger event themes**

The Munich bio-cluster also emerged in the context of significant preconditions and seeds, including some of the world’s oldest universities and RIs, a major pharmaceutical and chemical TNC sector, and extensive industrial manufacturing and electronics sectors

(Giesecke, 2000; Koehler, 1996).

Munich's bio-sector emerged in the wake of Genentech in the late 1970s, yet its development trajectory was heavily restricted by deeply rooted systemic weaknesses until the mid-1990s. Germany's PREOs were vertically structured and disjointed in nature, i.e. distinct separations of activities existed between universities and RIs, and they also had a pronounced basic research orientation as legal restrictions prevented PREO actors engaging in commercial activities. This prevented a PREO-based entrepreneurial mindframe from forming. Commercial developments were inhibited and undermined by the country's vertically structured TNCs absorbing researchers and commercially viable PREO research, and also by the Munich area's limited support ecosystem. Sectoral developments were also restricted by the absence of defined or direct Federal and/or State (Land) sectoral supports to explicitly drive commercial biotechnology-related developments (Chiaroni and Chiesa, 2006; Koehler, 1996).

Due to the high-risks involved, and the limited availability of support structures, particularly that of VC funding, Munich's first generation bio-firms adopted conservative platform technology activities/business models that were predominately based on US generated IP to exploit very narrowly defined niche market opportunities with German TNCs (Giesecke, 2000)

However, as with the UK Government, in response to European Union-wide developments seeking to address the dominance of the US bio-sector in the early 1990s, the Federal German Government introduced the BioRegio bio-cluster development initiative in the mid-1990s, choosing Munich as one of the programme's locations. This comprehensive sectoral development programme directly resulted in the Munich system's planned trigger event, through facilitating the rapid formation of a mass of bio-firms modelled on the 'Genentech template' by introducing intermediary actors, i.e. incubators and science parks, and public/private VC funds specifically focused on bio-firm developments (Chiaroni and Chiesa, 2006; Casper and Murray, 2005).

Despite the BioRegio programme's substantial supports, the Munich system has struggled to maintain a mass of commercial activity. This is due to the system's PREOs remaining vertically structured and disjointed, while the dominant actor type in the system's network structure are its TNCs. Additionally, the system's development

trajectory is being undermined by the new bio-firm developments being overwhelmingly platform technology-orientated in nature. An international mass of these bio-firms has formed, which is restricting opportunities for new bio-firm developments. Furthermore, an investment paradox has emerged, i.e. new bio-firms have experienced significant issues in accessing local VC funding, as the VCs are risk adverse due to the limited/restricted level of commercial developments (Chiaroni and Chiesa, 2006; DTI, 1999; Casper and Murray, 2005; Howells and Edler, 2011).

These issues are reflected in the system's anchor actor being the BioRegio programme's local coordinating organisation, BioM. The bio-cluster's brand has developed predominantly due to its association with the BioRegio programme, rather than through its commercial activities. This means the system's 'magnetism' is essentially confined to Germany and neighbouring countries. So far the bio-cluster has only attracted significant non-local PREO-based skills, competences and resources (DTI, 1999; Casper and Murray, 2005; Howells and Edler, 2011).

3.2.2 PBC system development issues

As stated, PBCs can be characterised as essentially being combinations of co-locating actors grounded in regional ambitions to become significant players in the global industry. As with bio-clusters, their trigger processes are case specific in nature. Yet, through analysing the development trajectories of a wide selection of international case studies, key themes of the main systemic and structural issues inhibiting and/or undermining their trigger processes can be identified, including issues relating to cluster specific policy initiatives. These themes are discussed in the following sections.

3.2.2.1 Key PBC systemic and structural weakness

As with bio-clusters, the development trajectories of PBC systems are strongly determined by the preconditions and seeds which form prior to their bio-sector's emergence. However, the existence of US, UK and German PBCs demonstrates that even where similar preconditions and seeds exist to those found in bio-clusters, they alone cannot facilitate a bio-cluster's emergence.

PBC trigger processes emerged through proactive private actor developments in the context of general non-sector specific industrial supports, and/or due to the introduction of defined public initiatives seeking to engender bio-sectoral developments. Yet, regardless of how their trigger process emerged, systemic weaknesses prevent an optimal development

trajectory forming. Key weakness themes can be identified throughout their value chains, whose nature and character are inter-related, and which reflect the inter-linked nature of the biotechnology innovation process.

PBCs typically have significant PREO infrastructures, yet an entrepreneurial development paradox may exist. Essentially, a PBC's PREOs may have a limited tradition of engendering innovative/entrepreneurial developments, which will inhibit the development of an entrepreneurial culture/mindframe and skills among PREO researchers and administrators. Such a scenario can develop for a variety of reasons, including the presence of established vertical structures among PREOs, the presence of established legal restrictions that prohibit academics from engaging in commercial developments, and/or the presence of poorly developed commercialisation support structures and systems, e.g. a country's IP and/or taxation regimes can inhibit entrepreneurial downstream developments due to perceptions of risk (Romanelli and Feldman, 2007; Giesecke, 2000).

These issues can impact on sectoral developments in several ways:

- significant public and/or private commercialisation supports will not develop due to a low PREO demand for such supports, which then feeds back into and further ingrains the limited PREO-based innovative/entrepreneurial developments;
- the general absence of commercialisation supports and/or infrastructures typically results in the adoption of risk adverse bio-firm business models in the limited cases where such developments occur, i.e. platform technology activities, whose defined activities limit up- and downstream links in the sectoral value chain, thus undermining a system's network structure development, and;
- limited PREO-based entrepreneurial developments will restrict/undermine downstream actor and sectoral developments, which paradoxically inhibit PREO-derived entrepreneurial developments due to a lack of downstream demand for commercially viable research and limited spillover opportunities and/or developments (Romanelli and Feldman, 2007; Giesecke, 2000).

Essentially, a conservative mindframe towards entrepreneurial developments becomes embedded throughout a bio-sector, limiting commercial activity and the development of a system 'brand'. This restricts a system's ability to attract in local and non-local labour, knowledge, resources. Indeed, limited sectoral activities can lead PBCs to loose key systemic competences and resources to more asset rich systems. Additionally, commercial

actors in a poorly developed bio-sector will seek alliances with actors in more asset rich locations in order to bypass indigenous systemic weaknesses. However, such strategies face significant issues as PBC actors come from systems with limited innovative images or reputations, and are competing with actors from more advanced/reputable systems for these resources (Powell et al., 2002; Gertler and Levitte, 2005; Zhang and Haiyang, 2011; Engel and Del-Palacio, 2011; Graf and Krüger, 2011; Eisingerich et al, 2012).

Another issue that can inhibit a PBC's development trajectory is where its system's structure is dominated be a TNC. Their vertical organisational structures limit potential alliances with other sectoral actors due to their closed network orientation, while their age undermines the development of an entrepreneurial culture due to limited institutional memory of engaging in new entrepreneurial developments. Additionally, their substantial resources and facilities can also absorb PREO research and skills, undermining key systemic spillover and spin-off developments from PREOs. Furthermore, where TNC FDI operations are present in a system, they may only form limited alliances with sectoral actors due to their limited autonomy (Powell et al., 2002; Gertler and Levitte, 2005).

3.3 ACTOR AND NETWORK TYPOLOGIES IN THE BIOTECHNOLOGY INDUSTRY

3.3.1 Sectoral Actor Typologies

In order to detail how biotechnology clusters emerge and operate, it is important to detail the main actor typologies of bio-sectors. These typologies are presented in Table 3.1, which is derived from observable patterns in the international sector (principally the US sector). This table presents an augmented and up-dated version of typologies developed by Barley et al. (1992), reflecting the changing roles and inter-actor relationships caused by the international bio-sector's evolution (Owen-Smith and Powell, 2007; Romanelli and Feldman, 2007).

It must be noted that all of the actor types detailed above are important in the functioning of a bio-sector's interactive value chain, by acting as either incubators or transfer mechanisms within the sector's innovation process, and are detailed separately for ease of presentation purposes only.

3.3.2 Formal and informal network typologies in the bio-sector

The following sections detail the main formal and informal network alliances found between the various actors in the international bio-sector's interactive sectoral value

chain. Many of the relationships in the bio-sector are informal and undocumented, yet those presented here are derived from observable patterns in the key international bio-sectors. These relationships can be considered as being generally applicable to the international bio-sector as a whole, yet they are reproduced in case specific manners (Barley et al., 1992; Romanelli and Feldman, 2007).

3.3.2.1 Typology of formal inter-actor networks in the biotechnology industry

Barley et al. (1992) identified ten key formal inter-actor relationships found in the international sector. These are presented in Table 3.2.

3.3.2.2 The main inter-actor network types in bio-sector value chains

The international bio-sector is an example of a complex, non-sequential network-based innovative high-tech Post-Fordist sector. The knowledge base from which biotechnology innovations draws is embedded in complex formal and informal networks between various actor types, including public research, government and industrial actors, while the development of biotechnology-derived products and processes involves many different formal and informal actor alliances, that have different spatial patterns, and which form at various stages in a product's and/or process's life-cycle (Morgan and Nauwelaers, 1999a; Owen-Smith and Powell, 2007).

As a broad generalisation, the biotechnology innovation process can be characterised as a tripartite alliance chain formed around the coordinated efforts of key actor types, i.e. Public Research and Education Organisations (PREOs), bio-firms (the bio-sector's innovation process linchpin), and downstream commercial actors, e.g. pharmaceutical TNCs. These actors create a non-linear, continuously interactive structure in which a hierarchy cannot typically form. Their interactions, which are supported and facilitated by region-specific support structures, act as feedback loops that update and alter the innovation process, optimising the process for the benefit of all network members (Malecki, 1997; Morgan and Nauwelaers, 1999a; Owen-Smith and Powell, 2007).

The following sections present a template of the bio-sector's networked structure, detailing the main formal and informal inter-actor networks found in the bio-sector's value chain, and also the evolution of formal downstream networks in the bio-sector. These relationships are derived from observable patterns in the US bio-sector, yet are replicated throughout the international bio-sector in case specific manners.

Table 3.1: The bio-sector actor typologies

Public Research and Education Organisations (PREOs): Commercial biotechnology developments in the international bio-sector are predominantly based upon findings from the research programmes of PREOs, they also facilitate complex tacit and codified information exchanges, and crucial sectoral skills developments and transfers. There are three PREO actors:

- Universities are the main source of the basic research from which commercial biotechnology activities are derived. Academic departments primarily focus on long-term speculative/exploratory basic research, which is important for volatile technology sectors, by being less subject to market pressures then commercial actors. Universities actively promote information transmission by adhering to "the [traditional] norms of the open information disclosure characteristic of public science" (Smith and Powell, 2004: 8) through lecturing, publications, and placements. They also provide undergraduate and research-orientated postgraduate education programmes.
- Public Research Institutes (RIs): Typically established by university academics in association with government departments/agencies to develop themed research programmes based on their areas of expertise, RIs typically locate in close proximity to their 'parent' university/universities. The focus mainly on applied research; many commercial developments originate from RIs as governments seek, internationally, to engender such developments though facilitating formal alliances with commercial actors via defined commercialisation supports and infrastructures.
- Research Hospitals (RH): RHs focus on specialised medical research, engaging in application-based diagnostic and therapeutic activities. RHs associated with a 'parent' university are typically located in close proximity. RHs are significant actors in the sector's innovation process by being the main source of clinical research trial samples, and are also involved in the clinical trials of new biotechnology-based therapeutics and diagnostics products, through joint research programmes with bio-firms and/or TNCs or via in-house laboratory research. RHs are among the main customers of biotechnology-derived pharmaceutical products and services.

PREOs increasingly seek commercial developments from their activities, and have developed advanced commercialisation procedures to optimise research transfers to commercial concerns. These mechanisms include pronounced commercial elements in education programmes to inculcate/encourage commercial mind frames among researchers, industrial liaison offices (ILOs) seeking to identify viable research into link into firm-based research programmes, technology transfer offices (TTOs) proactively seeking to transfer IP to commercial actors (some US and UK TTOs are independent entities whose survival depends on successfully commercialisation), and the development of bio-incubators (located in close proximity to RIs) to optimise firm developments through training, development, financial support services.

Biotechnology firms (Bio-firms): The bio-sector's innovation process, and key informal and formal networks, can be separated into two broad categories, upstream and downstream activities, relative to a firm's position in the sector's value chain. PREO research can be conceived as the upstream end of the value chain. Firms seek to engender informal and formal relationships with PREOs to access and commercialise research. The clinical trials process and sale to the consumer can be conceived as the downstream end, i.e. predominately formal network-based interactions with TNCs and other firms. Bio-firms traditionally occupy the middle rung in the sector's innovation process, being the main transferring mechanism of PREO research to the market. They draw on heterogeneous communities of experts at various points in their development, and are established by PREO researcher to pursue research exhibiting clear commercial promise to develop commercial products and services in a wide variety of research areas (yet, overwhelming in pharmaceutical-orientated research). Their development is determined through formal alliances with investor actors, particularly Venture Capital firms, to finance their start-up and initial developments prior to forming alliances with downstream actors. A firm's ability to access PREO-based knowledge and VC funding are the determinants of its research capabilities and its success in commercialising research through commercial actor alliances.

Investors: The technical and financial resources required to develop biotechnology products are beyond the capabilities of most bio-firms as, in comparison to other high-tech intensive sectors, development costs in biotechnology are significantly higher, e.g. product development can take up to 20 years and cost up to US$1 billion. Different investor types play particular roles in the product development process:

- Personal and Private funding sources: Due to their high risk nature, bio-firms often cannot access traditional finance sources, e.g. bank loans, meaning their set-up stages are often financed through personal and private funding, i.e. personal savings, private loans from friends/family, and non-business bank loans offset by the value of their intellectual property.
- Public and Private Venture Capital firms: VCs have played central roles in the international bio-sector's development since its inception. Typically established by wealthy private investors or by governments seeking to develop indigenous sectors, they target relatively unproven businesses traditional investors (e.g. banks) avoid due to high-risks or excessive development costs. VCs are compensated through equity securities in a firm in return for an investment, and thus a portion of capital gains when the firm is traded on stock markets through an Initial Public Offering (IPO) or bought up/bought into by a TNC (the main exit strategies for VCs in bio-sectors). VCs provide managerial and technical expertise to optimise a bio-firm's business development (academic researchers normally receive minimal education/training in business-orientated subjects), and new management structures can be sought to deal with the complexities of negotiating downstream alliances/collaborations. Several issues with VC funds motivates bio-firms *and* VCs to seek exit strategies, including a mismatch between the typical length of a VC alliance (5 years) and the biotechnology product/process development cycle's duration (approximately 15 years), while VC funding oscillates due to the relative performance of global economies and other industries.

Diversified Transnational Corporations (TNCs): TNC involvement in the international bio-sector predominantly focuses on pharmaceutical activities as the 'tradition' knowledge base they derived products from (organic chemistry) is reaching its technological development limits. Biotechnology draws from a different knowledge base (immunology and molecular biology) whose limits have yet to be clearly defined, and is easily adaptable to TNC requirements, meaning it is increasingly the basis of new pharmaceutical products/treatments. As the development costs and duration of new drugs is increasing due to stringent regulatory requirements, which impinge on TNCs recouping their development investments, and as effective patent-protection on traditional products is being impacted by generic products, TNCs are focusing on small volume niche market drugs, new versions of existing drugs, and have moved from mono-product to 'flexible' multi-product production. TNCs collaborate with bio-firms to optimise product development activities and fill their product development pipeline, which represent the main downstream relationships of the sector's innovation process.

Government Departments and Agencies: Many industrialised nations have identified biotechnology as key to their future economic development. Governments are increasingly crucial in providing funding to drive sectoral developments. Such funding can be typified as being primarily PREO focused, through resource and capital investment programmes/initiatives in the research capabilities and infrastructures of PREOs. Governments are also placing increased commercial emphasis on PREO activities to drive sectoral developments, and have created dedicated public VCs funds to address speculative funding shortages in sectors.

Additional actor types:

- Supply firms facilitate research and production activities, service suppliers provide specialised systems and solutions to different issues arising in research.
- Sub-national Biotechnology Centres are typically created by business associations to optimise a region's network structure and density, and disseminate important region-specific information among sectoral actors.
- Trade associations focus on specific sectors/sub-sectors, not particular locations, circulating sector-specific information and providing services to their members'. They can construct brands to improve a sector's profile, and act as lobbyists.
- Private Research Institutes are usually founded by wealthy benefactors to fund research in areas that receive little commercial attention, but are judged to have social value.
- Repositories (Gene Banks) are stores of genetic resources that seek to maintain genetic diversity by capturing a genetic picture at a particular point in time, and are important for future research projects, particularly genomic research.

After (Burke et al, 2003; Owen-Smith and Powell, 2007; Prevezer and Tang, 2008; Gertler and Levitte, 2005; Powell and Brantley, 1992; Barley et al., 1992; Stuart et al., 2007; Giesecke, 2000; Feldman and Braunerhjelm, 2007; Ernst & Young, 2007a; Ahrweiler et al., 2011; Lee, 2012; Eisingerich et al, 2012).

Table 3.2: Formal inter-actor network typologies in the biotechnology industry
Research grants are awarded to facilitate research programme developments by allowing researchers build and develop their research capacity. They typically have defined durations with a fixed funding award, and with clear ownership designation of the generated IP between the grant provider and receiver. They do not involve the division of non-research activities, e.g. marketing rights. They are primarily awarded to PREOs by Governments, while bio-firms and TNCs can award them in exchange for right of first refusal for licensing a project's results.
Research agreements (product development not involved) differ from research grants by covering more applied research activities. They are typically commercially sourced, e.g. bio-firms or TNCs commission researcher to conduct a defined research programme. They involve finance, resource and skill transfers. IP ownership is strictly defined between the members.
Research and Development (R&D) agreements are complex multi-actor agreements, where R&D activities are clearly defined among the participants (divisions of non-research activities, e.g. marketing activities, are not included). They agreements are important financial sources for bio-firms, due to their applied research focus, and involve formal and informal exchanges of resources, skills and codified information between agreement members. A bio-firm is the 'senior' partner, bearing most of the agreement risk/liability, while the 'junior' partner, e.g. a TNC, purchases a share of potential profit or loss, depending on the result(s) of a specific research programme. Initially, a 'junior' partner has minimal input in the research, yet as their relations and their underlying dependencies develop (i.e. relationships stratify as more defined roles and interactions develop), the 'junior' partner may demand increased input. Exclusive agreements can form resulting in the 'junior' partner buying into or outright purchasing the bio-firm, yet such developments are rare due to the complexity of the biotechnology innovation process.
Product development agreements (research activities not involved) involve information, resource and financial exchanges relating to the clinical evaluation, marketing, and distribution of a biotechnology-derived product/process. In such an agreement, a bio-firm would retain the patent rights of a product it developed in collaboration with a previous upstream PREO partner, while the product development partner, e.g. a TNC, would fund aspects of the product's development, acquire an exclusive licence to the product, and then pay the bio-firm product royalties on subsequent product sales. Joint ventures take on many forms, yet typically involve two or more actors collaborating on specific areas of a product's development process. Depending on an agreement's form, joint ventures can include joint research and/or development activity agreements, or take the form of two or more bio-firms creating new technologies and product lines through combining their resources and skills. In extreme cases, bio-firms may become contract laboratories for their joint venture partner(s).
Licensing agreements grant exclusive IP rights to a third party through an agreed fee or royalty rate. They occur at both ends of the product development process. Upstream agreements can follow the completion of a PREO-based project which displays commercial potential. The principle investigating scientist(s) may enter an alliance with an existing commercial concern through conveying the exclusive or non-exclusive right to use a particular scientific discovery's IP. Downstream agreements occur between a bio-firm and a TNC to compete a product's clinical trials process. Such agreements are the most important formal downstream alliance type in the bio-sector by determining IP ownership. Manufacturing and marketing agreements can also develop through such agreements.
Equity holdings/alliances take the form of alliances between bio-firms and VCs, or between bio-firms and TNCs. Typically they involve the partner actor becoming both a stakeholder and a shareholder in a bio-firm in exchange for financial investments. Alliances with VCs facilitate exchanges of business-related skills, while alliances with TNCs facilitate technological-related skills and resource exchanges.
Manufacturing agreements form between bio-firms and TNCs, and are strategically and economically motivated. They can form at the end of an existing development alliance, and, by granting them access to the established distribution systems of TNCs, bio-firms can by-pass the need to set up manufacturing operations/facilities.
Marketing agreements form after the successful completion of clinical trials. They grant an actor the marketing, supply and distribution rights to a product or technology, and can vary in their exclusiveness and expansiveness by being global agreements or territorially defined. They allow bio-firms' access the extensive marketing operations of TNCs.
Supply agreements develop where long-term relationships between actors, making a supply firm the primary supplier of a certain product or range of products to a customer.

After (Powell and Brantley, 1992; Roche, 2000; Krafft et al., 2011; Giesecke, 2000; Barley et al, 1992; Malecki, 1997; Visser and Boschma, 2002; Chiaroni and Chiesa, 2006; Prevezer and Swann, 1996; Bagchi-Sen at al., 2011).

Again, it must be stated that all actors are important in the sectoral value chain, and that while the inter-actor networks are detailed below in separate sections, divided into the different elements of the sectoral value chain, they are separated solely for ease of presentation purposes.

- **PREO-based research networks**

The bio-sector's innovation process begins with PREO-based scientists engaging in collaborative and exploratory basic research programmes, i.e. scientific experiments targeting a particular biotechnology-related theme/topic. Typically, such activities involve scientists collaborating on research relating to the biology of a particular disease/condition, and the drug targets (i.e. the genes, enzymes, receptors or other proteins that trigger or block biochemical processes within a cell) which are the best candidates to medically treat the disease/condition in question. The biological role of these targets in disease initiation or progression is validated in a process that may take upwards of 15 years to complete, and entails establishing if a deoxyribonucleic acid (DNA), ribonucleic acid, or protein molecule directly participates in a disease process

and is therefore a suitable target to develop a new therapeutic compound (Lawrence Berkeley National Laboratory, 2000; Malecki, 1997; Stuart et al., 2007; Lia and Gengb, 2012).

This stage of the innovation process is predominantly characterised by informal strategic, exploratory, and exploitative networks that involve exchanges of mainly filtered tacit knowledge and information, as well as exchanges of codified scientific and technical competences and skills, and research-related equipment and resources among PREO-based actors. Collaborative research programmes form through extensive inter-academic networks, developed and fostered by academics through their under- and post-graduate and professional careers, through industrial and/or PREO work placements, and through signalling their research credentials to the wider research community through publications and conference presentations (Malecki, 1997; Owen-Smith and Powell, 2008; Krafft et al., 2011; Lia and Gengb, 2012).

PREO research programmes can be characterised as being space specific agglomerations of tacit and codified scientific knowledge for two reasons. Firstly, the organisational structures and research capabilities of PREOs are dependent on their place specific research communities and infrastructures, which represent idiosyncratic local knowledge fields. Secondly, the information generated during a research programme's duration would be primarily held as researcher specific tacit knowledge, i.e. a research project would entail a specific methodological approach, background and training, and may originate from the findings of previous projects. This means that innovations are researcher-specific and do not transfer easily among different actors. The significance of the individual researcher in the innovation process is also compounded by the lack of overlap between the various areas of biotechnological research (Feldman, 1985; Prevezer and Swann, 1996; Breschi et al., 2001; Malecki, 1997).

Regional endowment of researchers, which are also place specific, determine the effectiveness of the filtering aspect of networks in localised learning processes, i.e. the manner in which local research is augmented by researchers accessing codified knowledge from non-local sources. By mixing local and global networks, researchers can complement a region's ‘‘local buzz’’, resulting in a more fertile innovation dynamic

through increasing idea diversity within a region's knowledge base (Gertler and Levitte, 2005; Graf and Krüger, 2011; Eisingerich et al, 2012; Huggins et al., 2012).

- **PREO networks with commercial actors**

PREOs actively promote information transmission and dissemination. As such, following the completion of a research programme, the generated tacit knowledge is ultimately codified through two principle avenues, which reflect a distinction in the commercial orientation of academics. Traditional research-orientated academic scientists predominantly focus on journal publications and/or conference presentations, while more overtly commercially minded entrepreneurial academic scientists will proactively seek commercial developments from viable IP generated from their research activities through seeking a patent development. The commercial orientation of academics, which is influenced by their previous career experiences, is regional specific and can be influenced by mimetic isomorphism (Casper and Murray, 2005; Murray, 2004; Zucker et al., 1998, 2001; Lundberg and Andresen, 2012).

Codification makes research findings available for licensing by commercial entities, e.g. bio-firms, or facilitates the creation of a start-up bio-firm (discussed further below) devoted to developing biotechnology-derived product and/or technique from commercially viable research. Licensing or start-up firm developments are the two main research commercialisation avenues in the international bio-sector (Lawrence Berkeley National Laboratory, 2000; Malecki, 1997; Visser and Boschma, 2002; Smith and Powell, 2004; Ahrweiler et al., 2011; Lundberg and Andresen, 2012).

The most common formal alliances between PREOs and commercial actors are licensing arrangements, followed by relatively limited collaborative R&D agreements, research agreements (with no development elements), and relatively minor research grants. Formal codified PREO relations with commercial actors, i.e. bio-firms and TNCs, are motivated by strategic and economisation motives of accessing their financial resources and technological capabilities to commercialise research. Additionally PREOs gain insight into industrial trends, needs and requirements, as well as information on breakthrough downstream research developments, and possible avenues for extra funding. Entrepreneurial academics seek to reap the financial returns successful commercialisation infers, and advance their alliances with downstream actors (Balconi et al., 2004; Sorenson, 2003; NESC, 1996; Giesecke, 2000; Lundberg and Andresen, 2012).

- **Upstream Bio-firm networks with PREOs**

Upstream alliances that bio-firms form with PREOs paradoxically represent the first downstream stage of the overall biotechnology innovation process, i.e. research findings enter the product development process. At this stage, PREOs represent the network structure's dominant actor type (Giesecke, 2000; Gertler and Levitte, 2005; Ozman, 2006; Feldman, 2000; Graf and Krüger, 2011).

As stated, bio-firms, internationally, are predominantly founded by entrepreneurial academics. As such, they often locate in close proximity to their 'parent' PREO. According to Malecki (1997), the process of entrepreneurship is geographically constrained as actors start new firms in areas related to their previous research activities and seek to continue the extensive formal and informal networks they previously enjoyed (Chiaroni and Chiesa, 2006; Morgan and Nauwelaers, 1999a; Ahrweiler et al., 2011; Eisingerich et al, 2012).

The relative geographic proximity and the degree of social inclusiveness of bio-firms to a PREO determines the degree to which informal relationships can be engendered, and facilitates access to commercially related and 'filtered' PREO-based tacit knowledge and sorted codified knowledge. Proximity also impacts on formal network formations. Through developing extensive explorative knowledge networks with PREO actors, bio-firms can surmount the high costs of searching for commercially promising research. The earlier a technology is licensed, the greater the level of exclusivity that is gained, which is crucial in determining a bio-firm's future earnings (Kostiainen Sotarauta, 2002; Ozman, 2006; Ahrweiler et al., 2011; Malecki, 1997; Eisingerich et al, 2012).

Overall, a bio-firm's ability to access, exploit and explore PREO knowledge sources determines its research capabilities, and directly influences its commercialisation activities. The filtering aspect of networks is increasingly important for bio-firms, internationally, as their research focus has intensified and become niche activity orientated. This development is due to the slowing pace and increasing costs of the biotechnology-derived drug development process, as detailed above. Additionally, bio-firms that form relatively more license agreements with PREOs are more likely to craft revenue-generating strategic alliances with downstream partners, as they will have more to offer (Romanelli and Feldman, 2007; Schweitzer et al., 2005; Feldman, 1985; Prevezer and Swann, 1996; Lundberg and Andresen, 2012).

This trend has deepened the importance of short distances and close social relations between bio-firms and PREOs, so as to generate suitable trust and reciprocity levels to facilitate knowledge and resource transfers. Where close social relationships form, informal and formal alliances are optimised by reducing informal transaction costs and insecurities through minimising the distance over which interaction and communication are conducted. This enhances inter-actor task coordination, codified resource and knowledge transactions and engenders knowledge spillovers (Feldman, 2000; Balconi et al., 2004; Sorenson, 2003; NESC, 1996; Rowley et al., 2000; Uzzi, 1996).

There are numerous non-contractual connections that bio-firms can engender with PREOs. These include a firm's founder(s) seeking to foster and deepen existing close personal contacts with academics, where a bio-firm is spun-out from PREO research, by maintaining academic appointments following its formation, the co-authorship of journal articles and conference presentations derived from collaborative research, through founders joining the scientific advisory boards of PREOs, through firms entering into/hosting study and work placements to facilitate competence and skill exchanges, and through collaborative training programmes (Chiaroni and Chiesa, 2006; DTI, 1999c; Morgan and Nauwelaers, 1999a; Erden and von Krogh, 2011).

Aside from research-based networks, bio-firms also seek to develop close networks with PREOs as skilled human capital may be sourced from and/or developed through interaction with them. Additionally, transfers of organisational routines, through formal business competence exchanges, may occur during the initial set-up phase of a bio-firm’s development, e.g. a bio-firm maturing in a PREO-based incubator may model its organisational routines and structures on those of its 'parent' PREO(s) (Owen-Smith and Powell, 2008).

- **Downstream Bio-firm networks with commercial actors**

Alliances between bio-firms and other commercial actors, e.g. other bio-firms and TNCs, represent the second downstream stage of the biotechnology innovation process, i.e. product development enters the clinical trials drug development process, detailed in Table 3.3 (Ernst and Young, 2000; Owen-Smith and Powell, 2007; Lee, 2012).

At this point in the bio-sector's innovation process, commercial actors assume the dominant actor role in networks. Different dominant actors in a wider network structure play particular roles as a sector matures and innovation becomes less radical, as such

bio-firm networks become predominantly formal in nature due to the codified nature of commercialisation-related interactions, and also as such relationships can form with non-local actors, e.g. TNCs (Gertler and Levitte, 2005; Owen-Smith and Powell, 2004; Soh and Roberts, 2000; Kogut, 2000; Graf and Krüger, 2011; Lee, 2012).

Table 3.3: The four phases of the clinical research trial process
The first phase involves the investigation of the safety of a product, its biological effects, its effects on the human metabolism, kinetics (i.e. the rates of chemical reactions), and drug interactions in a small human population sample of between 20 to 30 individuals. This phase can take up to two years to complete. Five drug/product candidates will typically enter this phase, of which 80% will pass.
The second phase investigates side-effect profiles, efficacy, and the dosage of a product on a large population sample of between 100 and 300 individuals who have the disease/condition under investigation. This can take two years to successfully complete, and only 30% of the drugs/products which enter this phase will pass.
The third phase investigates the reactions to long term use of a drug/product under investigation on a large sample of between 1,000 to 5,000 individuals who have the disease/condition under investigation. This can take up to four years, 80% of the drugs/products which enter this phase will pass
After the third phase, TNCs can then file an application with the relevant regulatory authority, e.g. the US Federal Drug Administration, to review and approve the product for sale. Only after approval is received can the producer commercially sell the product, although a further year of post-marketing testing is required to guarantee its safety. This represents the fourth and final stage of the clinical trials process.

After (Alliance Pharmaceuticals, 2002; Amgen, 2002; Élan Corporation, 2001; Ernst and Young, 2000).

Bio-firms initially adopt the structures of their 'parent' PREO(s), yet they will mimic and adopt the observable structures of successful bio-firms which have formed downstream alliances with VCs and/or TNCs as they develop, i.e. mimetic isomorphism will occur. Bio-firms will seek to develop structural similarities with successful bio-firms so as to facilitate similar downstream alliances through reducing perceptions of risk among potential collaborators (Owen-Smith and Powell, 2007; Slack and Hinings, 1994; Chen at al., 2011; Delerue and Lejeune, 2011).

The evolution of bio-firm networks from mainly open/informal to closed/formal forms is facilitated by formal (strategic, economising, exploitative and exploratory financial) resource and business knowledge/information networks between bio-firms and VCs. VC alliances facilitate the strategic development of firm-based commercially viable research, and result in the re-modelling of bio-firm management structures to optimise a VCs chosen exit strategy, as detailed above (Romanelli and Feldman, 2007; Schweitzer et al., 2005; Prevezer and Swann, 1996; Chen at al., 2011; Lundberg and Andresen, 2012).

Where VCs/bio-firms seek to enter formal alliances with a TNC, they wish to access the more advanced financial and technical resources of the TNC by forming market-oriented strategic, exploitative and economising research and business orientated networks that facilitate scientific and technological competence and resource exchanges (e.g. the vast regulatory experience of TNCs), and the development of marketing, supply, manufacturing, sales, and distribution networks. In such alliances, a bio-firm

offers prospective TNC collaborators its scientific capabilities, i.e. its ability to evaluate external scientific knowledge, and its technical capabilities, i.e. its ability to utilise external knowledge. The formal nature of these alliances mean bio-firms achieve relationship asymmetry with TNCs, while TNCs access and control a bio-firm's IP, and direct/influence the direction of its research programme(s) (Malecki, 1997; Ozman, 2006; Powell and Brantley, 1992; Casper and Murray, 2005; Chen at al., 2011).

Overall, bio-firms and TNCs create formal networks that enhance the sectoral innovation process by recombining new and old information in new ways. The nature of these alliances means their research teams establish close interactions, facilitating informal network developments as the level of trust and reciprocity develops/evolves. Both actors strategically seek to establish exploratory and exploitative information and resource networks to exchange skills, and tacit and codified scientific and business information/knowledge, as well as resource and procedural exchanges, so as to generate information spillovers (Visser and Boschma, 2002; Powell and Brantley, 1992; Lee, 2012).

Alliances between bio-firms and TNCs remain the international bio-sector's most optimal downstream alliance form, i.e. the 'Genentech template'. However, downstream alliances have stratified as the international bio-sector has matured.

The first bio-firms in the mid/late 1970s focused on large, non-niche targets as they experienced first mover advantage and faced little sectoral competition. Genentech's successes sparked a 'gold rush' mentality among VCs and TNCs, leading to many bio-firm developments internationally, which opened up non-US sectors. As such, TNCs and VCs could now be very selective in forming alliances, and could tailor research for themselves more optimally. Additionally, it became increasingly evident, as the 1980s progressed, that very few bio-firms could replicate/mimic Genentech's successes (Ernst and Young, 2001; Giesecke, 2000).

These issues established the niche nature of bio-firm activities internationally. They resulted in the downstream end of the bio-sector's innovation process fracturing, in combination with TNCs reorganising their Fordist structures to mimic bio-firm structures. Yet, the relative size of bio-firms, and their operations, to TNCs shrank due to their increasingly narrow research focus, making inter-firm alliances much easier and

equitable than alliances with TNCs. This development was, and continues to be, facilitated by the establishment of new bio-firm forms which focus on specialist technological and research support services, not on commercialising research, i.e. platform technology firms, which provide specialist tools to other bio-firms in order to assist their drug discovery research, and product development firms, which conduct specific aspects of the clinical trials process for customer bio-firms (Giesecke, 2000; Ernst and Young, 2001; McMillan et al., 2000; Forfás, 1999).

The networks which bio-firms develop with these service bio-firms resemble those found between bio-firms and TNCs, i.e. they are predominately formal in nature and feature codified exchanges of information and resources (McMillan et al., 2000; Forfás, 1999).

A related, though contrasting development is the emergence of second generation bio-firms. These emerge where an established bio-firm identifies new product platform or product development opportunities through its R&D programme(s), yet resource restrictions may prevent it from addressing/investigating these opportunities. As such, the parent bio-firm may spin-out a new, second generation bio-firm to continue (for example) a new research programme, without stretching the existing bio-firm's finite resources (Powell and Brantley, 1992; Ernst and Young, 2001; McMillan et al., 2000; Giesecke, 2000).

In this scenario, the 'parent' bio-firm becomes the dominant actor. Due to their origin, second generation bio-firms locate in close proximity to their 'parent' bio-firm so as to develop close informal and formal networks to facilitate exchanges of information, resources, personnel, and science and technological competencies. Additionally, they derive their research methodology, business ethos and management structure from their 'parent' bio-firm. In the international bio-sector, more mature bio-firms in-source technology developed from their second generation counterparts, yet this is a relatively rare occurrence due to the bio-sector's slowing development pace (Giesecke, 2000; Gay and Dousset, 2005; Graf and Krüger, 2011; Eisingerich et al, 2012).

Another alternative downstream strategy for bio-firms is where they re-invest earnings acquired through licensing agreements to either fund future research programmes, or to develop more advanced downstream capabilities, e.g. manufacturing or marketing

facilities, in order to allow the bio-firms to move down the product development process. These developments are motivated by the desire to retain more control over IP by restricting the level of interaction required with downstream partners, so as to retain a larger percentage of potential future financial returns. However, only a limited number of bio-firms have succeeded in developing such capabilities internationally (Cato Research, 2002; Scopa, 2000; Powell et al., 2005; Bagchi-Sen at al., 2011).

The changing nature of formal downstream bio-firm alliances has impacted on TNCs. Yet, as stated above, the downstream alliance demands of TNCs have also altered. In response to this increasing mismatch with niche focused bio-firms, TNCs have restructured their existing research operations and/or established biotechnology research laboratories to mimic the horizontal, network-based organisational structures of bio-firms. Several of the larger TNCs, e.g. GlaxoSmithKline, have also created virtually independent research operations that mimic the locational patterns of bio-firms, i.e. they locate in close proximity to PREOs in order to engender the same informal and formal networks found between PREOs and bio-firms (McMillan et al., 2000; Giesecke, 2000; Malecki, 1997).

These changing structures have led TNCs to seek licensing agreements with sectoral actors engaged in early stage applied research activities, i.e. recently established bio-firms, or directly with PREOs. This development has been facilitated by "...the availability of better prediction tools and more sophisticated methods for objective risk determination" (Ernst & Young, 2006a: 3), and is motivated by the limited number of bio-firms in the international bio-sector that are reaching the first stages of the clinical trials process. Coincidentally, start-up bio-firms are increasingly focusing on attracting TNC involvement, as they experience significant pre-clinical research funding issues due to on-going issues with 'traditional' sectoral investment sources, i.e. IPOs and VC funds, as detailed above (Ernst and Young, 2001; 2007a; McMillan et al., 2000; Giesecke, 2000; Powell and Brantley, 1992).

Overall, these developments mean two inter-related innovation network forms can be identified in the downstream end of the sectoral value chain, particularly in main global bio-sectors:

- 'traditional' vertical innovation networks between PREOs, bio-firms and TNCs,

i.e. where bio-firms act as the main mechanism in transferring PREO-based research results/findings to the market place, and;

- 'horizontal' downstream-actor innovation networks involving bio-firms, second-generation bio-firms, and bio-firm mimicking research entities of TNCs collaborating on network-based innovative activities (Malecki, 1997; Giesecke, 2000; Ahrweiler et al., 2011).

Horizontal downstream networks are focused on product developments, and are overwhelmingly formal in nature, as tacit and codified knowledge/information and resources are now predominantly held by commercial actors. This means that the relative importance of PREOs in downstream innovative developments decreases as a bio-sector matures, yet they remain crucial in generating the tacit and codified information/knowledge and skills that feed sectoral innovative developments (Gay and Dousset, 2005; Gertler and Levitte, 2006).

3.3.2.3 Networking patterns in the PBCs

The network structures and innovation processes of the global bio-clusters are the templates for the international bio-sector. They act like a collective entrepreneur, where sectoral actors form regional specific, dense concentrations/critical masses of complex and varied skills, resources, information and networks. These networks facilitate the rapid transfer and diffusion of information/knowledge and resources to engender sector-wide innovative developments, and feed the development of self-supporting and generating regional agglomerations (Anderson et al., 2004; Feldman, 2001; Malecki, 1997; Delerue and Lejeune, 2011).

In comparison, in order to compensate for actor weaknesses/absences and network/value chain weaknesses, a common strategy for PBC actors is to develop distant collaborative network strategies with actors in more knowledge and resource rich locations, optimally bio-clusters. Essentially, these actors seek to develop alternative forms of proximity. For example, Powell et al. (2002) suggest there are four key global VC centres, i.e. Boston, New York, the San Francisco Bay Area and San Diego (coincidentally bio-clusters). Many PBC firms seek alliances with VCs in these global centres in order to circumnavigate investor actor weaknesses in their own bio-sectors. Yet, they face significant issues in doing so due to the poor image/reputation of their bio-sectors caused by their limited innovative activities and developments (which paradoxically can be caused by their sectoral investor actor issues), and the intense

competition they face from more dynamic bio-sectors (Gilding, 2008; Casper, 2007; Zhang and Haiyang, 2011; Delerue and Lejeune, 2011).

Additionally, alternative proximity strategies involve considerable financial, logistical, and managerial costs due to the absence of local proximity and the sometimes significant distances involved. These issues can dissuade hub actors from entering into such alliances, meaning that the less endowed hub regions experience cumulative disadvantages, and fall further behind relative to bio-clusters (Powell et al., 2002; Gertler and Levitte, 2005; Morris, 2011; Delerue and Lejeune, 2011).

3.4 BIOTECHNOLOGY CLUSTER POLICY THEMES AND TEMPLATE

3.4.1 Bio-cluster development policy themes

The emergence and visible success of the international bio-clusters have encouraged different regional, National/Federal Governments and supra-national organisations to seek to engender similar developments in their own economies through different development strategies derived from observable patterns, processes and institutional arrangements in the established bio-clusters (Brown, 2000; Prevezer and Tang 2007; Avimelech and Teubal, 2007).

The following sections detail the role of Government initiatives in the emergence of the bio-clusters, and the main issues relating to the cluster specific policy initiatives seeking to engender cluster emergence in the PBCs.

3.4.1.1 The role of Government initiatives in the emergence of the international bio-clusters

Government initiatives have played case specific roles in directly or indirectly facilitating the emergence of the global bio-sector's bio-clusters.

The US bio-clusters emerged in the context of substantial US Government investments in seeding general factor conditions and related and supporting industries, particularly the Cold War era funding initiatives which created the advanced and specialised infrastructures of the country's PREO base and the entrepreneurial support ecosystem which exploits the commercial promise these PREO investments engendered, so as to facilitate developments in the wider economy. These initiatives indirectly seeded a defined entrepreneurial/innovative culture which, in combination with the complex nature of the support structures, facilitated and drove the exploitation of the PREO-based developments, and established a positive path dependence that optimised the US

bio-sector's development trajectory (Anderson et al., 2004; Bagchi-Sen at al., 2011). However, a key feature of the US bio-clusters is that a complex set of predominantly private actor driven, mutually reinforcing and aligned interests emerged in the context of indirect, though aligned, public interests and supports that fostered the development of the bio-clusters' value chains, and drove their trigger processes (Anderson et al., 2004).

The continuing indirect nature of the Federal initiatives exists due to the established absence of a specific Federal body to oversee sectoral developments. Yet, the Federal Government has continuously addressed issues restricting sectoral developments since the US bio-sector emergence, e.g. the Bayh-Dole Act (1980) addressed issues restricting the commercial exploitation of PREO research which emerged through the surge in US bio-sectoral activity that followed Genentech's emergence. Federal Government developments continue to focus on optimising the national entrepreneurial environment/ecosystem as a whole, and are not specifically focused on the US bio-sector (Giesecke, 2000: Romanelli and Feldman, 2007).

The absence of a sector-specific Federal industrial development programme has been a key factor in the development of tailored bio-cluster system governance structures and ecosystems. The development of these ecosystems continues to be driven by indirect State Government initiatives that focus on regulation and entrepreneurial ecosystem fine tuning. Essentially, State Governments have adopted cluster informed approaches that are tailored through public/private dialogue processes that include sectoral lobbying efforts and input from regional trade associations, which focus on system specific adjustments to respond to the evolving needs/requirements of a system. This approach seeks to induce continual, structured and self-reinforcing process of growth and development through on-going innovative and entrepreneurial activities (Giesecke, 2000: Romanelli and Feldman, 2007; Porter, 1998; Lundberg and Andresen, 2012).

Examples of such measures include the introduction of specific skills and competence building exercises to improve a system's specialised factor and demand conditions, and the fine tuning of a bio-cluster's legal and regulatory environment, e.g. changes to tax regimes, to improve the strategies and structures of a system's bio-firms, and its related and supporting industries. The indirect nature of these initiatives means that no comprehensive State level/regional development strategies have been developed in the

US, and that no specific typologies of cluster informed policies can be derived (Romanelli and Feldman, 2007; Feldman and Braunerhjelm, 2007; Wolfe and Gertler, 2007).

In relation to the EU bio-clusters, their pre-conditions and seeds developed in the context of different Government structures, i.e. the National and Local Government structures in the UK, and the different Federal and Land Governments in Germany. Additionally, both countries are members of the EU's supranational structure (Lewis et al., 2001).

The UK's National Government had developed proactive efforts to engender advanced high-tech sectoral developments prior to Genentech's emergence. Local Government activities were primarily extensions of these initiatives. The National Government's initiatives engendered a national PREO-orientated entrepreneurial environment that facilitated the emergence of pharma-TNC and NICT/electronics agglomerations in the Cambridge area, i.e. positive path dependence elements (i.e. factor conditions, demand conditions, firm structure and strategy conditions, and related industries) were in place to facilitate and drive the bio-sector's positive development trajectory.

In Germany, significant Federal and Land investments had facilitated the development of an advanced PREO base. Yet, despite Germany being the first country, internationally, to introduce a defined biotechnology specific PREO research funding programme in the early 1970s, it failed to establish a significant biotechnology-orientated research base. This was due to the Federal Government's limited understanding of biotechnology resulting in the programmes formulation process being dominated by existing PREO researchers, meaning the programme failed to address the then emerging field of genetic engineering. Additionally, restrictions preventing academics entering into commercial developments, and the established vertical PREOs structures, undermined the development of an entrepreneurial mindframe and/or a tradition of collaborative alliances among academic and commercial actors (Giesecke, 2000).

The Cambridge and Munich bio-sectors emerged following Genentech's foundation, yet their development trajectories were undermined by system specific weaknesses, as detailed above. The UK Government introduced defined sectoral development

initiatives in the early 1980s to address the lack of VC involvement in the bio-sector, which facilitated the development of an agglomeration of bio-firms. No public initiatives were introduced in the German bio-sector, meaning very limited sectoral developments occurred nationally.

Both EU bio-clusters emerged due to the introduction of planned Government structures whose introduction was motivated by EU-driven efforts to address the increasing dominance of the US bio-sector. The UK government initially formulated cluster specific policies derived from observable patterns in the US bio-sector that engaged with the Cambridge bio-sector's existing actors and structures and facilitated the bio-cluster's hybrid trigger event (Cooke, 2002; Department of Trade and Industry 1999; Casper and Karamanos, 2002).

The Cambridge bio-sector's initiatives have become increasingly more tailored and attuned to the bio-sector's individual needs and requirements. Nationally, sectoral specific policies continue to be developed and implemented through dedicated agencies, including the Biotechnology and Biological Sciences Research Council, and through sectoral specific initiatives of the Department of Trade and Industry (Invest UK, 2001: Department for Environment, Food and Rural Affairs, 2007).

The German Federal Government's BioRegio programme is responsible for the Munich bio-cluster's emergence, through introducing substantial commercial development infrastructures and supports, in particular dedicated VCs. The BioRegio programme was designed on observable patterns in the US bio-sector, yet formulated and tailored to the German bio-sector through a Federal consultation process that involved State Governments and key sectoral actors (Casper and Karamanos, 2002; Cooke, 2002).

Unlike in the US, where the different governance structures inter-link to continuously seek to optimise the Federal ecosystem and address State specific issues through public/private cluster informed approaches, the different governance structures in the EU bio-clusters are disjointed and remain hierarchical/public actor dominated. These issues undermine their development trajectories:

- in the Cambridge bio-cluster, the limited integration between the different governance levels is reflected in the presence of National regulatory issues

undermining the bio-cluster's entrepreneurial developments, including limited clarity in the UK's patenting regime, and issues relating to the country's taxation regime, and;

- the Munich bio-cluster's on-going development is locally managed through the public/private structured BioM organisation, yet it is not integrated with existing Federal Governance structures, as reflected in the continuing systemic weaknesses caused by the hierarchical PREO structures (Casper and Karamanos, 2002; Cooke, 2002).

In comparison to their US counterparts, Casper and Murray (2005) characterise the EU bio-clusters as being more entrepreneurially conservative due to the more central role public initiatives play in their development, while their system structures are characterised by vertical structures, limited inter-actor networks and systemic spillover events. These issues undermine their development trajectories. As with the US bio-clusters, the specific natures of their systems means that no specific cluster informed policy typologies can be derived (Casper and Karamanos, 2002).

3.4.1.2 PBC cluster specific policy issue themes

Many Governments have identified biotechnology as being strategically important for their country's future economic development. In many PBCs, as well as the Cambridge and Munich bio-clusters, cluster specific initiatives were initially developed through analyses of observable patterns in the established US bio-clusters. However, the German Government's BioRegio programme, itself derived from US sectoral observations, has become the template for the development of cluster specific initiatives since the turn of the century (Gilding, 2008; Wolfe and Gertler, 2007; Enright, 2000).

PBC development initiatives can be characterised as being public actor dominated developments that are formulated with limited private actor involvement, and which are derived from snap shots taken of established bio-clusters. They seek to engender specific and rapid sectoral developments determined and based upon election cycles in order to justify the sometimes substantial investments made by these initiatives. Public supports ultimately seek to advance sectoral activities to a point where private actors organically enter a bio-sector, so as to engender a self-sustaining bio-sector system (Anderson et al., 2004; Rochepeau, 2004; Venning and Yukawa, 2010).

Such programmes are typically implemented over two main stages that focus on

addressing big issue topics, i.e. initially they seek to address PREO infrastructural and resource weaknesses in order to drive sectoral developments by generating commercially viable research, and subsequently they focus on facilitating transfers of this commercially viable research to new and existing commercial concerns by addressing limitations in sectoral commercialisation support infrastructures and resources, such as the absence of VC actors (Anderson et al., 2004; Venning and Yukawa, 2010).

This focus on big issue topics can result in systemic development surges/expansions in relation to what existed prior to their introduction, yet their large target orientation can fail to surmount and/or fully address complex systemic bottlenecks/weaknesses, i.e. missing skill sets and/or resources, for a variety of reasons.

Public initiatives can be characterised as being reactive in nature as public actors are directly removed from industrial development trends. This means that the essentially top down nature of PBC development initiatives can fail to address intricate and complex systemic weaknesses which can be embedded in the institutional characteristics of a PBC's actors, and/or exist due to their organisational structures, through imposing impracticable and/or unsuitable initiatives.

As stated above, cluster specific initiatives typically focus on facilitating new commercial developments originating from PREO-based research through introducing early stage commercialisation supports. Yet, these supports fail to address existing private actor restrictions, including the conservative business models of existing bio-firms or the commercialisation support and investor actor funding limitations that downstream actors can face. This is due to such pre-existing downstream issues being viewed by public actors as being solely the domain of the private actors. Yet, the presence of innovation and entrepreneurial development paradoxes among established downstream actors will undermine sectoral developments.

Furthermore, as cluster specific initiatives are typically formulated with limited private actor involvement, vested interests can dominate their formulation, thus undermining their suitability to fully address the specific issues present in a bio-sector (Anderson et al., 2004).

Additionally, the PBC case studies demonstrate that cluster specific initiatives mainly

focus on engendering defined niche focused platform bio-firm developments due to their relatively less risky and more predictable nature, in comparison to drug development/product orientated firms. This is in response to the expanding costs and duration of the drug development clinical trials process. This focus seeks to achieve rapid sectoral advances within a defined time period, yet while such a focus can indeed result in an initial surge of bio-firm developments, their limited nature propagates a risk adverse systemic 'environment' that restricts up- and downstream spillovers and sectoral developments (Anderson et al., 2004; Casper and Murray, 2005).

As such, the envisaged level(s) of entrepreneurial developments fail(s) to emerge, meaning that time lags develop between the introduction of the initial supports and when public actors realise that deeper levels of intervention and longer time scales than previously initially envisaged are required. This is a common problem evident in most of the PBC case studies.

The introduction of more advanced resources and initiatives usually involves more substantial input from private actors so as to formulate and introduce more system-specific, tailored, and intricate initiatives. However, the disjointed, stop-start nature of PBC development trajectories remains. The fractured build-up of sectoral supports results in more modest commercial development levels, relative to the private actor driven systems, as initiatives are insufficient to facilitate the optimal growth of PBCs in the medium to long-term as they remain tied to political election cycles. This is increasingly problematic as the economic, technical and development timelines and risks associated with the bio-sector are increasing, i.e. target/goal driven approaches are increasingly unsuitable to optimally contain the evolving associated risks of biotechnological developments.

Target-based initiatives can also distort markets through seeking the achievement of set targets regardless of their suitability to a bio-sector. An extreme example is the strong Government involvement in the Chinese bio-sector. Due to strictly defined targets and political/cultural factors, no bio-firm can fail. This has distorted the Chinese bio-sector's market by feeding systemic lock-in developments and undermined the development of the bio-sector's entrepreneurial ecosystem (Giesecke, 2000; Prevezer and Han Tang, 2007; Graf and Krüger, 2011).

Furthermore, questions over the long-term sustainability of platform bio-firm orientated

development strategies are developing as a critical mass of such firms is forming internationally. This issue relates to Governments deriving their initiatives from similar 'templates', i.e. the US bio-sector and the BioRegio programme, and it is further compounded by Governments seeking to engender sectoral developments in the context of the evolving and on-going development of established bio-clusters. Essentially, cluster specific initiatives are playing catch up with the bio-clusters, as well as trying to counteract the rising threats from cheaper and more specialised locations in the Far East and Southern Hemisphere that are offering lower production costs, strong science bases, and vast internal markets (Casper and Murray, 2005; Giesecke, 2000; Europe Innova, 2008).

3.4.2 Cluster specific policy themes to facilitate bio-cluster developments

The limited number of global bio-cluster developments directly associated with cluster specific initiatives, and the nature of the observable PBC's structural weaknesses, demonstrates that public actor initiatives cannot solely create bio-clusters.

The German Government's BioRegio programme demonstrates that a comprehensive policy framework can establish national research agendas, introduce key infrastructures and institutions through specialist factor investments, and can also engender an entrepreneurial support ecosystem through micro-economic policy measures that optimise the development of existing and new system activities and engender the formation of inter-actor networks. Yet, the BioRegio programme also demonstrates that such a framework cannot fully address a system's existing path dependence, i.e. established institutional characteristics, structural weaknesses, and/or a poor commercial culture/entrepreneurial environment which undermines entrepreneurial and innovative developments (Cooke, 2002; Feldman and Francis, 2002; Delerue and Lejeune, 2011).

The Cambridge bio-cluster case study demonstrates that cluster specific policies only succeed when they mesh with an existing system that forms in the context of substantial place-specific preconditions and seeds, and whose trigger process emerges over a period of decades through a system-specific development trajectory that involves a wide variety of complex and idiosyncratic interactions of competences, skills and resources held predominantly by private sectoral actors, in the context of a supportive ecosystem (Romanelli and Feldman, 2007; Wolfe and Gertler, 2007; Lee, 2012).

These issues demonstrate that in order to fully address the evolving demands of a PBC system, cluster specific initiatives should be formulated and introduced through a long-

term, responsive and adaptive policy framework which optimally builds upon strengths, and addresses weaknesses present in the four determinants of competitive advantage. Such a framework must be constructed through an open ended inclusive dialogue process that involves all the relevant public and private sectoral stakeholders, so as to tailor initiatives towards building on pre-existing competences and productive systems and to increase the ability and capacity of a system's actors to absorb innovation investments and resources. This issue has clear implications for the relationship between public actor technology/innovation and industrial policy strands (Porter, 1998; Asheim and Isaksen, 2002; Oughton, Landabaso and Morgan, 2002)

Such an inclusive dialogue process can be a challenge for highly-regulated/vertically structured Governments, yet it is required as a cluster system's skills, competences and resources must ultimately be private actor in nature. Additionally, the long-term inculcation of a coordinated systems-based entrepreneurial/innovative support ecosystem that suitably addresses all the demands and requirements of the bio-sector's characteristic interactive tripartite sectoral value chain cannot form solely through traditional 'top down' initiatives, as Governments are often directly removed from market forces and are at best reactive in nature (Anderson et al, 2004; Leydesdorff, Cooke and Olazaran, 2002; Porter, 1998; Casper, 2007; Feldman and Braunerhjelm, 2007; Erden and von Krogh, 2011)

Through using bio-cluster and PBC case studies, the policy recommendations detailed by DTI (1999) and Anderson et al. (2004), as well as the entrepreneurial and innovative functional resource (EIFR) requirements list presented in chapter 2, a template of cluster specific policy themes can be presented that both facilitate and drive entrepreneurial and innovative developments throughout a bio-sector's value chain (Casper, 2007; Romanelli and Feldman, 2007; Wolfe and Gertler, 2007).

3.4.2.1 Knowledge infrastructure, resources and skills

PREO generated scientific knowledge is the starting point of the bio-sector's value chain and innovation process. The technical capabilities and resources available to PREO scientists strongly determines a bio-sector's commerciable research activities by influencing start-up bio-firm and biotechnology-derived product and process developments. As such, a strong PREO science base is a key element in engendering the conditions which facilitate a bio-cluster's ultimate emergence (DTI, 1999d; MacPherson, 1998; Prevezer 1997).

Wolfe and Gertler (2007) comment that one of the soundest PBC policy programmes is the introduction of sustained investments in building the infrastructural base and education capabilities of a PBC's PREO actors, i.e. to develop a complex array of modern facilities and high-tech equipment resources so as to generate high-levels of basic research and industry-orientated applied research in a wide variety of biotechnology/biotechnology-related areas, and to develop a highly qualified skilled labour force. Such developments are required, as the quality and character of the research capabilities, skills, and (sticky) knowledge sets of a PBC's PREOs are key elements in the synergy processes that influence a system's development trajectory due to the existence of local learning processes, technology transfers and spill-over effects supported by geographic and cultural proximity (Malecki, 1997; Anderson et al., 2004; Casper, 2007; Anderson at al, 2004; Krafft et al., 2011; Engel and Del-Palacio, 2011).

On its own, a strong science base will not facilitate a cluster's emergence, yet a weak science base will undermine innovative and entrepreneurial developments and a PBC's development trajectory. This issue directly relates to the development of advanced and specialised factors which are necessary to enhance a system's production capabilities, capacity, and accumulation of technological capabilities. In order to address hierarchical and disjointed organisational structures and limited cross actor interaction, initiatives must focus on developing cross institutional and inter-disciplinary infrastructural and administrative structures so as to facilitate inter-PREO actor knowledge exchanges and spillover events. Such infrastructures require the alignment/coordination of different technological platforms, which can result in more efficient use of resources, e.g. preventing unnecessary duplications of facilities and/or resources, and optimise the development of higher quality research and skills development programmes (Swann and Prevezer, 1996; Prevezer 1997; Cooke, 2002; Feldman and Braunerhjelm, 2007)

PREO education programmes strongly determine a system’s ability to develop a suitably skilled labour force. This influences key network developments and inter-actor knowledge exchanges, key elements in the synergies which facilitate cluster emergence. A highly educated and skilled labour force feeds the growth of local enterprises and can ultimately attract non-local actors, and their skills, competences and resources, into a PBC as they seek to access a system's advanced PREOs. As such, PREOs must develop education courses that are tailor-made to address the various complex and evolving labour demands of a PBC's actors. This requires close and continuous collaboration

between PREOs and a system's actors in designing such programmes (Wolfe and Gertler, 2007; MacPherson, 1998; Anderson et al., 2004; Casper, 2002; Graf and Krüger, 2011; Eisingerich et al, 2012).

Allied to skills development activities, initiatives should also focus on the retention of skills and competences in PREOs, particularly where a 'brain drain' occurs, so as to avoid undermining a system's development trajectory through skills flight to more asset rich bio-sectors. Initiatives should also be developed to attract local researchers back into a system from non-local research positions, as well attracting in non-local PREO actors to seed alternative skills, and competences. In order to foster and embed such developments, such initiatives require strategies to prevent potential 'belligerent' reactions from local researchers, as well as the presence of suitable PREO research infrastructures and resources, and a suitably advanced level of downstream actor activity (Anderson et al., 2004; Casper, 2002; Koehler, 1996; Engel and Del-Palacio, 2011; Graf and Krüger, 2011; Eisingerich et al, 2012).

3.4.2.2 Entrepreneurial infrastructure, resources and skills

The engine of a PBC's trigger process, and the linchpin in its value chain, are the entrepreneurial and innovative activities and developments of a system's bio-firms. The presence of a growing bio-firm base is a crucial aspect in the successful development of a bio-sector as it creates several key cumulative benefits. Commercialisation advertises a system's innovative capacities and supports, encouraging increased system-based entrepreneurial developments, and can also attract non-local skilled labour, supports, and actors into the system (Compete, 2005; OECD, 2004; Porter, 1998; Romanelli and Feldman, 2007; Graf and Krüger, 2011).

A system's entrepreneurial infrastructure and supports, and the psychological and/or social characteristics of its actors determines its innovative and entrepreneurial propensity. Such elements are optimised where a multi-faceted long-term support system, comprised of a complex range of 'hard' and 'soft' resources and infrastructural supports, develops through public/private interactions so as to support entrepreneurial/innovative developments and experimentation throughout a bio-sector's value chain (Compete, 2005; Anderson et al., 2004; Owen-Smith and Powell, 2007; Malecki, 1997; Lundberg and Andresen, 2012).

A PBC's entrepreneurial resources should seek to engender conditions which facilitate and drive the transmission of knowledge from PREOs to downstream actors, and provide the

flexibility and support for new entrepreneurial developments through reducing entry barriers. This includes developing supports that seek to prevent 'lock-in' events forming as technological and/or organisational structures evolve through facilitating entrepreneurial experimentation, i.e. the development of new business models. Bio-firm developments are themselves idiosyncratic entrepreneurial experiments as their forms, structures and activities are unique in nature and are determined by the system in which they form. Additionally, such supports should seek to encourage the adoption of biotechnology-related processes among existing and related industrial sectors in order to facilitate new industrial applications in areas that complement the 'core' activities of a bio-sector (Wolfe and Gertler, 2007; Anderson et al., 2004; Europe Innova, 2008; Engel and Del-Palacio, 2011; Lee, 2012).

'Hard' entrepreneurial sectoral supports are detailed in Table 3.4.

The commercial orientation of PREO actors is crucial in determining technology transfers to commercial concerns, through influencing the commercial orientation of research programmes and the nature and character of knowledge spillovers with commercial actors. These issues influence a PBC's development trajectory, as where an established entrepreneurial culture is not present among PREO actors, the perceived/actual risks associated with commercial developments will deter academics from seeking such developments. Additionally, the quality and range of the commercial-orientated routines that actors acquire during their PREO careers will strongly influence the commercial orientation and development trajectories of bio-firm developments (Klepper, 2001; Kostiainen and Sotarauta, 2002; Casper, 2002; Owen-Smith and Powell, 2004; Ozman, 2006; Lundberg and Andresen, 2012).

To address such issues, a series of value chain and entrepreneurial coaching/mentoring services should be developed, optimally in partnership with private actors. Such services could also be developed through introducing skilled non-local actors into PREOs so as to seed the relevant skills, e.g. through temporary placement programmes. At a minimum, commercialisation skills should be introduced as pronounced elements in established under- and post-graduate education programmes. Further options include the development of technology transfer and entrepreneurial coaching lectures, seminars and/or tutorial initiatives, and management training programmes to seed even basic entrepreneurial skills among new and existing PREO researchers and administrators (Feldman, 1985; Cooke, 2002; Anderson et al., 2004; Engel and Del-Palacio, 2011; Graf and Krüger, 2011).

Table 3.4: 'Hard' entrepreneurial sectoral supports
Structural bridges between PREOs and downstream actors should be engendered to optimise knowledge exchanges and spillover developments, as the interface between PREO/commercial actors is a central element in a sector's value chain. As such, legal issues restricting PREO actors from commercial activities or entering commercial alliances or information exchanges with downstream actors should be addressed.
A suitable IP regime to facilitate commercial developments through reducing perceptions of risk and uncertainty. For PREO actors, the nature of a IP regime can engender further commercial developments by influencing potential financial returns from successful commercial developments (through, for example, licensing agreements), and can advance their careers, depending on the internal promotion structures of PREOs. For bio-firms, the commercial potential of their IP is often one of a limited number of tangible assets they possess prior to the successful development of their products/processes. The strength and quality of a bio-firm's IP will significantly impact on potential alliances with downstream actors, i.e. VCs and TNCs.
Infrastructural supports can be introduced to encourage commercial developments, including the provision of suitable laboratory space to allow the optimal development of commercially viable research, and business development services/incubators. Such developments could be introduced and implemented as complementary elements, yet should include technical supply services that allow actors access modern high-tech instrumentation and premises through temporary leasing arrangements and flexible leasing arrangements.
Structural and resources issues among the PREO technology transfer offices (TTOs) must be addressed to improve commercial transfers. Anderson et al. (2004) suggest the introduction of specific commercialisation structures to proactively drive PREO developments, including the restructuring of TTOs as independent commercial entities whose survival depends on proactively scouting for commercially viable research, and the incubation of potential commercial developments through innovation funding to motivate PREO actors to exploit commercially viable IP they develop.
As biotechnology is capital intensive, private investor actor weaknesses/absences must be addressed. Such issues can create an investment paradox, i.e. conservative modelled firms cannot attract the interest of risk adverse investors as their inability to develop significant commercial developments dissuades investors from forming alliances with them. Public VCs/investment funds are often developed to address such issues, yet typically underperform due to the limited entrepreneurial mindframe/culture among actors and the conservative nature of public investors. As such, a wide range of public investment funds should be developed, optimally with private actors. These include a public credit system (to prevent struggling, though viable firms from bankruptcy), loan guarantees, and dedicated seed funds. These funds require realistic, not target/goal focused approaches, as the quality of commercial developments is important for a bio-sector's development trajectory, not the quantity. Funding should be allocated through a competitive tendering process (where appropriate) to ensure a high quality level is maintained. Proactive efforts should also be made to attract private investor actors through the development of public/private investment partnerships, potentially from related high-tech sectors to facilitate spillover developments.

After (Cooke, 2002; Anderson et al., 2004; Casper, 2002; Kaiser, 2002; Engel and Del-Palacio, 2011; Wolfe and Gertler, 2007).

Such programmes could be extended and tailored to downstream actors, in particular pre-existing bio-firms, in order to facilitate the development of their management and business structures. New and existing bio-firms require the presence of varied marketing and sales competencies, and specialist legal actors for complex licensing and co-operation negotiations. These supports could be developed through involvement from a panel of local and non-local experts from industry and academic positions. Such developments are important, as (for example) the quality of a bio-firm's technical and general business expertise strongly influences their ability to attract the attention of potential VC collaborators (Giesecke, 2000; Anderson et al., 2004; Casper, 2002; Eisingerich et al, 2012).

3.4.2.3 Inter-actor networks

Inter-actor networks are central elements to the international bio-sector's innovation process and its intricate tripartite value chain, as the generation and communication of tacit and codified knowledge occurs through reciprocal, interactive, and strategic up- and down-stream alliances between sectoral actors (Barley et al., 1992; Romanelli and Feldman, 2007; Erden and von Krogh, 2011).

The presence of extensive inter-actor networks is crucial for developing a bio-cluster's internal logic, and engendering the conditions which facilitate a system's trigger event, including spillover developments. Networks facilitate the distribution and dissemination of different forms of filtered information, and impact on a system's development trajectory in

numerous ways, including mimetic isomorphism. Additionally, networks are central elements in the nature and character of the EIFR ecosystem and play a key role in a PBC's public/private dialogue process (Owen-Smith and Powell, 2004; Ozman, 2006; Ahrweiler et al., 2011; Lundberg and Andresen, 2012).

Yet, network developments can be problematic in bio-sectors where there is a lack of understanding of the concept of inter-actor networks and their associated benefits, or where collective action issues undermine their development, e.g. where an innovation paradox exists (Forfás, 2004; Anderson et al., 2004; Lundberg and Andresen, 2012).

As such, network developments in a bio-sector should be sought through a programme that coordinates a mixture of induced and organic processes which seed the concept of networks amongst a bio-sector's actors by allowing them gain a theoretical and practical understanding of the capabilities of networks to facilitate or constrain future actions and market opportunities. Such a programme should involve a broker programme/service that identifies potential networks and encourages their 'artificial' development, thus facilitating interaction and learning synergies, in combination with the provision of financial supports to encourage actors to embrace cooperation. Ultimately, such a programme seeks to induce naturally/organically occurring private actor network developments, yet as this requires the development of inter-actor trust and reciprocity, central elements of inter-actor networks, such efforts require a long-term approach (Ffowcs-Williams, 2000; Martin and Sunley, 2001; Casper, 2002).

3.4.2.4 Market information exchange resources

Cluster specific initiatives should be formulated and implemented through a public/private actor dialogue process. Yet, in order to address existing information gaps which could undermine such a process, it is important that cross-system exchanges of information occur through information exchange resources. Such resources should include intermediary institutions and actors, including cross-cluster discussion forums, and intermediary technology transfer resources, so as to optimise a PBC's internal synergy by engendering mimetic isomorphism and spillover developments facilitated by, and based on inter-actor networks (Anderson et al, 2004; Wolfe and Gertler, 2007, Owen-Smith and Powell, 2007; Zhang and Haiyang, 2011; Lundberg and Andresen, 2012).

Cross-cluster discussion forums should draw from a bio-sector's support actors, i.e. its

regional development organisations, trade associations, and supply actors. Such forums can facilitate the development of business and competitive intelligence supports and services to optimise a PBC's development trajectory by collecting and disseminating filtered and up-to-date information, including early movement signals, on a system's skills, markets, business and clinical development trends (Porter, 1998; Romanelli and Feldman, 2007; Zhang and Haiyang, 2011; Engel and Del-Palacio, 2011).

For PREOs, these supports and services can allow the optimal development of commercially oriented research programmes, and can feed into the formation of an entrepreneurial mindframe. For new and existing bio-firms, such supports and services can engender a variety of benefits including the formation of related business activities in a PBC system, allowing firms to optimise their research activities, e.g. scientific advisory boards can emerge where experts provide scientific trajectory/development advice, and facilitate the development of new business models. Such developments will influence the nature of, and their ability to enter into alliances with investors and/or downstream actors (Anderson et al, 2004; Casper, 2002; Lundberg and Andresen, 2012).

Such services and supports require the presence of a certain level of activity in a bio-sector's value chain, including the presence of service and supply actors, a solid cluster management structure, and the presence of an established inter-actor network structure in order to regulate actor behaviour, due to the importance of confidentiality and privacy of company and research data (Anderson et al., 2004; Lia and Gengb, 2012).

By establishing discussion forums, a system 'brand' may form or be introduced, which can impact on a PBC's regional and international visibility. A brand can feed into the development of cross-cluster cooperation initiatives to stimulate the circulation of non-local information in order to boost a system's development trajectory, and prevent systemic 'lock-in' developments (Romanelli and Feldman, 2007; Owen-Smith and Powell, 2007; Engel and Del-Palacio, 2011; Graf and Krüger, 2011).

A common manner in which bio-sectors seek to boost their international presence is the development of a biotechnology directory, a promotion/marketing tool to foster networks and knowledge exchanges nationally and internationally. Optimally, a directory should be established and run by a neutral organisation, e.g. a public agency, to address confidentiality issues. Such an organisation should be charged with

developing a detailed database to inform the directory, as well to establish international conferences (Anderson et al., 2004; Wolfe and Gertler, 2007).

The establishment of a directory could link in with the creation of skill development programmes to address a bio-sector's existing skills and competences shortages, as well as international placement and recruitment programmes. Furthermore, a directory could link in with the establishment of consultation/advice boards that identify common issues among different systems, cross-pollinate skills so as to stimulate a system's entrepreneurial and innovative developments. Such developments would encourage economic diversification to prevent systemic 'lock-in', by addressing limitations in the diversity of a domestic knowledge base (France BIOTECH, 2001; Romanelli and Feldman, 2007; Owen-Smith and Powell, 2007; Engel and Del-Palacio, 2011; Graf and Krüger, 2011).

Cluster specific initiatives should proactively seek the establishment of technology transfer intermediary institutions, i.e. science parks and incubators, to create geographically concentrated information exchange nodes between PREOs and downstream actors. Such institutions facilitate key value chain network and spillover developments through supporting the generation of market-focused IP and the emergence of PREO-based entrepreneurial developments. As such, they are key elements in the development trajectory of a PBC system (Wolfe and Gertler, 2007, Porter, 1998; Casper, 2002).

While these intermediary actor types typically require public investments due to their high costs, public/private actor involvement is required in their design as, aside from the provision of office and laboratory space, equipment and materials, they must focus on providing a complex range of added value technological services, e.g. project feasibility studies, market research, business management, and legal services. The nature of their support infrastructures are crucial, i.e. they should be temporary in nature to support, not prop up commercial developments, and should evolve so as to reflect changing sectoral and firm development requirements (Anderson et al., 2004; Carlson, 2007; Lundberg and Andresen, 2012).

Bio-incubators should be created as commercial entities whose survival depends on successful alliances and commercial developments so as to engender a pronounced commercial emphasis/orientation to their activities. In some cases, more extreme

incubator structures are created e.g. in the Munich bio-cluster, each bio-firm development is allocated a unique 'commercialising company', which is a specially tailored commercial entity that seeks to optimise a specific bio-firm's commercial development (Daskalakis and Kauffeld-Monz, 2007; Kogut, 1988).

Science parks can be either themed or general in nature, yet they are centres of collaborative commercial research which bring together government, PREO and commercial actors so as to engender collaborative innovative activities and to facilitate entrepreneurial spin-off developments in cutting edge technologies, such as biotechnology. As such, they facilitate crucial transfers of PREO/commercial actor knowledge and information in the context of extensive, tailored research and commercialisation infrastructures, resources and skills (Anderson et al., 2004; Malecki, 1997).

While intermediary actors are associated with new commercial developments, several PBCs have introduced intermediary actors that also focus on facilitating and supporting the commercial exploitation of PREO-based IP in existing bio-firms. Existing bio-firms are targeted to address existing innovation paradoxes, typically through the provision of funding to issues that restrict their ability to develop more advanced innovative activities (Anderson et al, 2004).

Intermediary actors feed into the skills development aspects of knowledge and entrepreneurial infrastructure, resources and skills. By developing common infrastructures, inter-actor PREO-based information exchanges can occur, allowing researchers from other areas to interact. Additionally, due to the close proximity to commercial actors, 'dual ladder' career paths can be developed to allow academics and/or commercial actors move between the different actors, i.e. flexible/permeable industry-academia interactions, to facilitate tacit knowledge exchanges and spillover developments. Furthermore, the development of incubators and science parks can feed into a PBC's branding, and assist in attracting in non-local skills, competences and resources to boost a system's development trajectory (Anderson et al., 2004; Malecki, 1997; Graf and Krüger, 2011; Eisingerich et al, 2012).

3.4.2.5 Actor and institutional density, and skill, competence and resource depth

A PBC's development trajectory is optimised where a structured self-reinforcing process

of growth and development is facilitated and driven by the formation of a diverse range of market and non-market actors and institutions and associated competences and resources throughout the bio-sector's value chain.

This depth and density is important in setting the overall context or framework in which cluster development takes place and forms, due to the other EIFRs engendering an adaptive and responsive ecosystem that facilitates and drives entrepreneurial and innovative developments and interactive synergies (Porter, 1998; Maskell and Kebir, 2005; Wolfe and Gertler, 2007; Casper, 2002; Howells and Edler, 2011).

Where such density and depth forms, due to the range of skills and resources and the level of entrepreneurial and innovative activities and opportunities present in a system, the local ecosystem can facilitate second generation bio-firm developments, while also attracting in non-local sources of labour, knowledge, resources and finance, particularly from non-local private VCs and TNCs. Such developments facilitate significant positive systemic feedback inputs, including spillover developments (Malecki, 1997; Wolfe and Gertler, 2007; Engel and Del-Palacio, 2011; Ahrweiler et al., 2011).

Optimally, systemic depth and density should form organically. However, cluster specific policies are unlikely to facilitate such developments through initiatives alone, as evident in the Munich bio-cluster, yet efforts can be made to engender coordinated networks of interconnected actors, and facilitate systemic externalities through an 'anchor' actor strategy. There are three anchor actor strategies, i.e. a system organised around the organic development of a 'star' actor, a system organised around the facilities of TNCs, and an interdependent model where a PBC and a TNC play interdependent roles (Anderson et al., 2004; Howells and Edler, 2011).

Cluster specific initiatives can seek the development of a successful ‘role model’ bio-firm, i.e. a local bio-firm that successfully develops a commercialised biotechnology-derived product, to demonstrate the commercial potential and depth of a system's support structures to internal and external actors. Such a bio-firm can stimulate “...entrepreneurship among scientists in research centres...[encouraging commercial] exploitations of research results” (Chiaroni and Chiesa, 2006: 3) to develop commercial activities, thus further enhancing the entrepreneurial culture of a system (Prevezer and Swann, 1996; Scott, 2007; Kolympirisa et al., 2011).

In relation to the second strategy, despite TNCs being central elements in a bio-sector's value chain, the PBC case studies demonstrate that no such strategy, internationally, has been adopted. TNCs are typically viewed as being an element, not the central element, of cluster specific strategies, in part due to the limited influence governments have over them, yet also as TNCs undermine a system's development trajectory due to their size and scale where they are a system's dominant actor, e.g. the New York City PBC (Anderson et al., 2004; Baik, 1997; Doherty, 2001; Gilding, 2008; Graf and Krüger, 2011; Lee, 2012).

Essentially, the embeddedness of TNCs in a PBC's system is crucial in determining their impact on the system's development trajectory. As such, where TNC-related developments are sought, initiatives seek to embed organic systemic developments in parallel with/to encourage more complex TNC activities, i.e. an interdependent model. To attract significant TNC operations into a system, a PBC must have the combined presence of key PREOs, a global leadership in focused research areas with recognised health-care application(s), and also have effectively managed bio-firms with relevant leading-edge technologies and IP suitable for R&D investment, i.e. a sustained and innovative bio-sector needs to be present. Optimally, where a TNC enters a system, it will achieve a strategic alliance with a comparably sized innovating partner, i.e. an emerging/emerged bio-cluster system (Porter, 1998; Brown, 2000; Biggerio, 2002; Ahrweiler et al., 2011; Lee, 2012).

3.5 CONCLUSION

The international bio-sector is an example of a complex network-based innovative high-tech sector. The value chain in leading bio-sectors is characterised by tripartite network alliances between PREOs, bio-firms (the value chain linchpin) and TNCs. The knowledge base from which biotechnology innovations draw upon is embedded in complex formal and informal networks between various actor types, including PREO, public and industry actors. The downstream end of the value chain is comprised of two inter-related, parallel vertical and horizontal aspects that involve different types of bio-firms, i.e. drug discovery and service/platform technology firms, and TNCs.

This complex network structure has been supported and facilitated by the development of extensive regional specific public and private sectoral supports. These include regional specific tiers of specialist supply firms, sub national biotechnology centres, and trade associations that are attuned to the demands of the region's actors.

Geographic variations in regional endowments of bio-firms, institutions, and social capital means there exist significant differences in how the bio-sector's innovation process is replicated internationally. Where dense agglomerations of actors, competences and resources form, bio-clusters can emerge, i.e. a mode of organisation of a productive system that contributes to the level of innovation and competitiveness of its constituent actors (Engel and Del-Palacio, 2011; Huggins et al., 2012).

The emergence of bio-clusters, and the benefits associated with them have encouraged Governments internationally to seek to engender such developments where they have not emerged. However, bio-cluster systems are born and develop on the basis of case specific combinations of capabilities, incentives, and opportunities. The language used to describe the factors which determine bio-cluster development and emergence is vague/ambiguous, e.g. pre-conditions, path dependence/development trajectory, feedback and spillovers; meaning there is very little that is tangible, or strictly definable for policy measurements to be developed upon. Generalisations drawn from case studies are inadvisable due to the case specific nature of bio-cluster systems, however case studies play a particular role in identifying key parameters and relationships, and place policy recommendations/suggestions in their proper theoretical background.

Bio-cluster specific policies should seek to develop the relevant pre-conditions and 'seedings' that can ultimately facilitate and encourage a bio-cluster's emergence. Policy initiatives must include a strong science base, the foundation and the starting point of the bio-sector’s value chain, and the development of an entrepreneurial culture, a key requirement in the emergence of a critical mass of entrepreneurial activity. The development of inter-actor networks is vital due to the networked value chain, while the strength of a country’s bio-firm base and support 'eco system' are all key elements in a bio-sector’s internal dynamics.

As such, policy initiatives seeking to engender bio-cluster developments require a coordinated, supportive long-term systems-based approach, that is tailored to the evolving needs and circumstances (including chance/serendipitous events) of the bio-sector in question through a public/private dialogue process, so as to create a suitable policy environment that facilitates the development of the various conditions that lead to bio-cluster emergence and development. Essentially, an evolutionary, systems-based

approach towards policy formulation and implementation is required.

CHAPTER 4:
METHODOLOGY

4.1 INTRODUCTION

This chapter describes the methodology employed in compiling a detailed profile of the Irish biotechnology sector (bio-sector), and in identifying and analysing the network arrangements that exist in the indigenous bio-sector. The chapter is divided into four sections. The first section sets out the project's research question. The second section details the methodology used in compiling a profile of the bio-sector's actors. The third section describes the design and implementation of a questionnaire designed to obtain specific information on the networks that exist between the biotechnology firms (bio-firms) and the other actors in the indigenous bio-sector. The final section outlines the approach taken in conducting interviews with key sectoral actors informed by the process of compiling the sectoral profile and through the completed questionnaires.

4.2 THE RESEARCH QUESTION

The empirical research in this thesis was guided by the following general research question:

What networking arrangements exist among the actors in the Irish bio-sector, and what inter-actor networking strengths and weaknesses exist in the bio-sector that impact on its on-going development?

Answering this question required the compilation of a detailed profile of the indigenous bio-sector, under four general key headings:

- the Irish bio-sector's actors,
- the bio-sector's inter-actor networks and interactions,
- the functions, performances, and weaknesses of inter-actor sectoral networks and clusters in Ireland in relation to their international counterparts, and
- existing Irish Government policies relating to the indigenous bio-sector.

The manner in which this profile was compiled is discussed in the following sections.

4.3 METHODOLOGY EMPLOYED IN CONSTRUCTING THE SECTORAL PROFILE

4.3.1 Analysis of secondary documentation

> "There is a lack of data on the existence and extent of industry-industry networks in Ireland" (Forfás, 2004: 43).

The profile of the Irish bio-sector's actors was constructed using an augmented and updated version of the bio-sector actor typologies developed by Barley et al (1992), as presented in chapter 3 (Barley et al., 1992; Romanelli and Feldman, 2007).

Literature relating to the indigenous bio-sector and its activities is in short supply. In terms of compiling a general profile of the bio-sector, InterTradeIreland's *Mapping the Bio-Island* (2003) report was invaluable. This report detailed the activities, locations, and the scale of operations of bio-firms on the island of Ireland.

Additional information on the bio-sector's composition was derived from the BiotechnologyIreland.com website in 2004 and 2005. This website proved invaluable with respect to all aspects of the profile as it is the central hub of on-line information regarding biotechnology-related activity in Ireland, and includes a database of registered individuals and firms in all aspects/areas of Irish biotechnology and biotechnology-related activity. The site is hosted by Enterprise Ireland (EI), and is home to Enterprise Ireland's Biotechnology Directorate (EIBD), EI's life science and food commercialisation group.

The accuracy of the information contained in the InterTradeIreland report and the Biotechnology Ireland website was rigorously cross-checked against information from the websites of the individual bio-firms using the Google search engine. This procedure identified several inaccuracies in both of the main sources, and identified a small number of bio-firms not listed in either source. It was established that a small number of bio-firms had no web presence, or were not mentioned in material obtained from government agency literature/web sites. Contact with a senior academic in a National University of Ireland, Maynooth's (NUIM) Department of Biology with extensive national and international sectoral experience clarified the activities of these bio-firms. This academic's advice was sought for clarification of subsequent ambiguities and inconsistencies that were encountered during this stage of the research.

The next phase in creating the sectoral profile involved compiling an inventory of the biotechnology/biotechnology-related activities of Irish Public Research and Education Organisations (PREOs). Using the Google search engine, a detailed review of the activities of the relevant academic departments and their key researchers, along with their research interests, was carried out. In addition, an inventory of the relevant

biotechnology/biotechnology-related courses provided by these institutions was also compiled.

This stage of the research also involved detailing the activities of the various research institutes (RIs) affiliated with the country's academic departments, as well as other privately and publicly funded RIs. The bulk of this information came from EIBD, the BiotechnologyIreland website, and the review of the activities of University Departments. A report by the US-based New Economic Strategies group, *The Global Reach of Biotechnology* (2003), provided additional information on several of these RIs.

Further information on a small number of RIs was obtained from a web search using Google. Due to the complex nature of the biotechnology/biotechnology-related activities in which these departments and RIs are engaged, several areas of ambiguity were again addressed through discussions with the senior academic. This stage of the profile also involved an investigation of the biotechnology-related activities of the main Irish hospitals, which was completed using web-based information.

As part of the review of bio-firm- and university-based activities, details on the activities of the various Government departments and agencies which oversee biotechnology/biotechnology-related sectoral activity were also assembled. Literature from relevant Government departments and web-based sources, such as agency websites, and the aforementioned New Economic Strategies report were used to complete this section of the research.

The next stage of the research involved identifying the various investors in the bio-sector. Literature from EI and the IDA Ireland was used to identify biotechnology-related investors, such as venture capital (VC) and seed capital funds, while a major web-based search uncovered other potential investors, mainly investment funds created by the main banking/financial institutions in the country. A series of discussions with a senior academic in the NUIM's Department of Economics with significant experience in international business identified further investor related areas, and clarified ambiguities that had developed.

Following the completion of this stage of the review, a profile of the biotechnology-related operations of diversified Transnational Corporations (TNCs) in Ireland, typically

involving pharmaceutical or biopharmaceutical activities, was constructed using information from the InterTradeIreland report, literature from IDA Ireland and EI, and relevant company websites.

The final stage of the profile involved the compilation of an inventory of suppliers of goods and services to the indigenous bio-sector. This was compiled using the InterTradeIreland report, the Biotechnology Ireland website, and also through a rigorous search of web-based material derived from a detailed review of these sources.

4.3.2 Questionnaire of bio-firms

In the course of compiling the general profile of the indigenous bio-sector, it became apparent that the bio-sector loosely imitated the structure found in the US bio-sector, as detailed in chapter 3. However, while similar networks of interactions and collaborations can be identified, their size and scale are much smaller. However, the degree of complexity of the interactions and collaborations in the bio-sector, even at this early stage of the profile, was apparent.

Originally, it was intended to flesh out the structure of the bio-sector via structured interviews with key personnel from the bio-sector's various segments. However, following an analysis of the limited secondary material collected during the course of the research detailed above, it was felt that the complexity of networks in the bio-sector necessitated a more comprehensive information search.

Accordingly, it was decided to conduct an initial postal questionnaire of all sectoral bio-firms. The questionnaire aimed to investigate the exact details of the key formal networking arrangements that had developed among these bio-firms, and would then be followed by interviews with key individuals in these bio-firms that were identified through the review of secondary information sources and the questionnaire findings.

A postal questionnaire, created using the procedure set out in Dillman (2000) as a guide, was issued to the 40 bio-firms identified during the sectoral review (the questionnaire, and a detailed description of the purpose of the questions, is presented in Appendix A). The questionnaire sought to elicit basic information about the bio-firms and to identify, in a systematic way, the formal and informal networks between the bio-firms and other sectoral actors. Specific bio-firm information was sought through the use of structured

questions, while respondents were also given the opportunity to voice their opinions on specific areas/topics and to elaborate their rationale/explanations where necessary. This information would also facilitate a more focused and informed subsequent interview process.

The design of the questionnaire proved to be rather time-consuming, due mainly to difficulties in properly structuring and wording sections covering the types of collaborations/alliances formed in the bio-sector. These sections required specific information to be included in the questions (for example, a definition of what is an International Corporation) to remove any possible ambiguity so as to allow the respondents to accurately answer the questions.

The draft questionnaire, when completed, was passed to the senior Department of Biology academic who assisted in the completion of the sectoral overview. As this individual was removed from direct involvement in the research project, a fresh perspective was brought to the questionnaire. On this individual's advice, minor changes were incorporated into the questionnaire.

In order to test the robustness of the questionnaire, a pilot version was issued to a select grouping of bio-firms identified in the sectoral review. Following a detailed analysis of their replies, no further changes to the questionnaire were deemed necessary.

4.3.2.1 Questionnaire administration

The next stage of the questionnaire process involved sending an introductory 'pre-note' to the remaining target bio-firms that were not part of the pilot questionnaire. This pre-note, as specified by Dillman (2000), informed the recipients of the aims of the questionnaire, and asked for their assistance in completing it. A week later, the questionnaire and a detailed cover note, explaining in summarised detail the aim and objectives of both the questionnaire and the entire research project, were posted with an accompanying self-addressed envelope to the target firms (the questionnaire letters and correspondents with the target firms are presented in Appendix B).

Following a two-week period, a lower number of responses than expected were received. 'Thank you' notes were issued to those bio-firms which had responded, and reminder notes issued to those who had not yet replied. The reminder notes emphasised the importance of the research and encouraged the respondents to complete and return

the questionnaire. The response to this stage of the questionnaire was very low.

After a short period of time, replacement questionnaires were issued to the bio-firms which had not replied. A small number of bio-firms requested replacement questionnaires following the issuing of the reminder note. Once again the response rate proved lower than anticipated. In a small number of cases, contact details provided on bio-firm web sites proved to be out of date. Accordingly, new questionnaires were issued to these bio-firms once their details were updated.

As stated, the questionnaires were issued to 40 bio-firms, of which 16 replied. It became apparent that, despite the successful results of the pilot questionnaire, a small amount of ambiguity existed in specific questions. For example, in Question Four, respondents were asked for the proportion of scientists/technologists employed, in several cases a figure was provided with no indication if this was the number of scientists/technologists in the bio-firm, or a percentage of the total employed by the bio-firm. However, issues of ambiguity were limited as not all of the respondents fully completed the questionnaire, which meant that an overall comparison between the answers provided for several questions was not possible. These issues were ultimately addressed through the in-depth interviews with the bio-firms.

4.3.2.3 Questionnaire analysis

As stated, 16 bio-firms replied to the questionnaire from the 40 which were issued. This was a much lower response level then anticipated, yet the completed questionnaires proved very useful in backing up the findings of the sectoral profile and in tentatively identifying sectoral trends.

The completed questionnaire returns were analysed in two stages. Firstly, sequential lists of the individual answers as they appeared in the questionnaire were compiled in order to identify general patterns among the respondents. This analysis confirmed several findings of the sectoral profile, e.g. that the bio-firms were mainly small in sized (the overwhelming majority of the respondents employed less then 20 people), and that despite the majority of respondents employing very large number of scientists, very limited product developments had occurred.

Secondly, a more focused analysis was conducted where the respondents were grouped according to their core activities, as identified in the sectoral overview, in order to

identify inter-sectoral trends or patterns (Table 4.1 details the numbers of respondents by their activities). This analysis also confirmed findings of the sectoral profile, e.g. formal linkages between the bio-firms and other actors in the bio-sector's value chain were very limited, and that the main area of sectoral activity was largely confined to diagnostic-/platform-related bio-firms. The questionnaires also proved very useful in identifying target bio-firms for the interview stage of the process.

Table 4.1: Questionnaire respondents activity focus	
Pharma-Biologicals	2
Pharma-Services	4
Diagnostic	6
Agri-food	3
Bio-Environmental	1

4.3.3 In-depth interviews

4.3.3.1 Organisation of the interview process

Using the completed sectoral profile and the completed questionnaire returns, a list of target actors for interview was compiled. Initially, this interview process was to focus on three different target groups:

- key actors from the different PREOs, i.e. universities, RIs, hospital-based RIs, and the Institutes of Technology,
- bio-firms, TNCs, and sectoral investors (e.g. VC firms), and
- government agencies and the remaining sectoral actors.

The rationale behind this segmentation of the research process was that it would allow for a more detailed analysis of the information generated about the specific target groups, which would then inform the formulation of the questions for the subsequent interview segments.

Requests for interviews were emailed to the targeted actors. This email (presented in Appendix B) contained a brief summary of the aims of the entire project, and provided a brief description of the topics that would be discussed in the interview.

The first target group involved key actors from Irish PREOs. As PREO-based research and PREO/bio-firm relations are the bedrock on which the biotechnology industry is founded, as detailed in chapter 3, it was important to document the experiences of the PREO actors in conducting research. Additionally, it was important to document their

experiences in forming linkages with bio-firms in Ireland, and (where relevant) abroad, in order to fully understand the initial stages of the biotechnology innovation process in Ireland.

The bio-firm actors were predominantly selected following an analysis of the questionnaire returns, and also through a review of company literature and websites. Some additional target interviewees were identified during the course of the first set of interviews with PREO personnel. The target TNC, and speculative investor interviewees were also identified in the process of compiling the sectoral profile, and through the first set of interviews.

The second part of the interview process proved to be very difficult to complete. Initially this stage was expected to be completed within a couple of months, but ultimately took over six months to complete due to a very low response rate among targeted actors, particularly among TNCs and speculative investors. Many efforts were made to contact TNC operations in Ireland, yet the response rate was extremely low, in part due to their branch plant nature. Several approaches had to be made to contact key TNCs, in particular Wyeth and Genzyme, before interview requests were granted. Following several unsuccessful attempts to contact speculative actors, the senior academic in the Department of Economics facilitated several contacts with investor actors.

The third stage of the interview process with government agency actors aimed to develop an understanding of the bio-sector as viewed by these actors. Initially, this section was planned to be initiated only after the previous interview stage had been completed, so as to compare the experiences of the other sectoral actors to the aims and objectives of the state agencies, yet due to the delays caused by the poor response rates in the second stage of the interview process, the phased interview approach was ultimately abandoned. However, the initial decision to delay this final stage of the process proved to be successful, as clear differences were identified between the intent and opinions of the government agencies and other sector commentators.

The remaining actor types identified in the course of the research were also included in this phase. As the number of suppliers of goods and services to the indigenous bio-sector are limited, this part of the process proved relatively straightforward to complete.

4.3.3.2 The interview approach

The interviews were conducted through a mixture of a structured open-ended approach and an interview guide approach, where specific topics were examined in each interview section. This mixture allowed for the recording of information on a fixed set of topics, thus facilitating comparison between interview returns, while also allowing for variations in actor responses/experiences, depending on case-specific circumstance and idiosyncratic information (Kitchin and Tate, 2000).

The interview process sought to explore the informal networking arrangements of the various sectoral actors in the indigenous bio-sector, and also sought to seek further information on, and the c*larification* of, issues identified during the sectoral review and the firm questionnaire analysis.

Those interviewed were also asked to identify key actors they felt would be able to expand/elaborate on certain comments they made. Due to the small size of the bio-sector, many actors (particularly Government agency actors) had established significant sectoral contacts, or had experiences of working in different areas of the bio-sector. This 'snow ball' process identified additional individuals and actors which/who had not been identified during the completion of the sectoral review. Several of the topics in question seemed to have a tenuous relationship to the purpose of the research project, yet when put in the context of the information gained during interviews, the links involved became more pronounced. This part of the interview process was vital in gaining extra insight into the functioning of the bio-sector.

The interview stage of the research also drew attention to a range of additional literature and documentation relevant to the bio-sector which had not been accessed during the previous stages of the project. These related in particular to sectoral reports, funding sources, and programmes prepared and sponsored by the European Union and other Europe-wide bodies. This literature fed into, and facilitated a more informed interview process, and enabled a more accurate and detailed appraisal process, allowing the material gained from the interviews to be placed in its proper Irish and European contexts.

4.3.3.3 Problems encountered

The main issue experienced in this stage of the research was the sometimes quite significant time lag between a request for an interview being made and the prospective

interviewee agreeing to the request. In certain parts of the bio-sector, in particular in relation to TNCs and private speculative investors, very low response rates were received. These response rates were addressed somewhat by altering the wording of the interview request email sent to the selected individuals, i.e. by removing any mention of the degree being pursued.

In a small minority of cases, individuals did not fully understand the geographic approach to the overall project, despite it having being detailed in the email request. This misunderstanding seems to have been due to a preconceived notion that only a student from a business/economics faculty would be interested in the subject area. In situations where this arose, a certain amount of time was spent addressing this misunderstanding/misconception.

In relation to the request for the interviewees to identify prospective additional interview candidates, in most cases individuals were willing to suggest several individuals or provided contact details of future potential interviewees, yet in a limited number of cases this request was met with significant resistance, possibly due to confidentiality issues. However, as mentioned, due to the small size of the bio-sector, many actors (particularly Government agency actors) had established significant contacts throughout the bio-sector, which proved useful in addressing knowledge gaps in certain areas of sectoral activity.

4.3.3.4 Interview analysis

A total of 54 interviews were conducted with sectoral actors (a detailed break down of the respondent numbers and their activities is presented in Table 4.2). After the completion of each interview, a full transcription was completed. A detailed analysis of each transcript was then conducted using the NUD-IST (Non-numerical Unstructured Data Indexing Searching and Theorising) programme to compile a representative picture of the experiences of the individual actor, and to identify issues to be discussed further in subsequent interviews.

This material, framed within the theoretical framework presented in chapters 2 and 3 and the wide reaching literature review (as detailed above), was rigorously studied so as to generate the findings and policy recommendations presented in the remainder of the study. Following the completion of each interview stage, the transcriptions were divided and grouped into sequential lists of the general topics discussed during the different

stages. This identified general trends and patterns amongst the sectoral actors. Subsequently the transcripts were divided into groupings determined by areas of common sectoral activity, where such distinctions were applicable, in order to identify subsectoral patterns. After the completion of the entire interview stage of the research, a major review of the interview transcripts was completed so as to tease out issues relating to potential policy suggestions.

Table 4.2: Interview respondents and activities	
PREO Administrators (including TTO and ILO actors)	7
Biotechnology/biotechnology-related Department actors	9
Research Institute actors	9
Research Hospital actors	2
Institute of Technology actors	1
Pre-initiative bio-firms	8
Post-initiative bio-firms	5
TNC actors	3
Investor/VC actors	3
Government agency actors	3
Trade Association actors	2
Supply actors	2

4.4 SUMMARY ACCOUNT OF INFORMATION FROM THE DIFFERENT RESEARCH STAGES

This chapter has described the methodology involved in compiling a profile of the indigenous bio-sector and of its main actors, through using an updated version of the template of actor typologies developed by Barley et al (1992).

The first stage of the research involved a review of secondary literature/documentation and an internet search with a view to detailing the actor typologies evident in the indigenous bio-sector. From this stage of the research, knowledge gaps in the full range of activities in the bio-sector were predominantly addressed. The review detailed patterns of sectoral activity and detailed the extent to which the various sectoral actors are interlinked through formal alliances.

The second stage of the research involved a postal questionnaire of sectoral bio-firms that sought to detail the formal networking arrangements between the bio-firms and the actors in the bio-sector's value chain. There were 16 respondents from a total of 40 posted questionnaires. The questionnaire returns demonstrated that the bio-firms were mainly small in size, engaged in limited activities mainly in diagnostic-/platform-related

areas, and that they had established very limited networks with actors in the bio-sector's value chain.

The third and final stage of the research involved detailed structured interviews with key sectoral actors, the aim of which was to detail the opinions and experiences of the various actors on/of the bio-sector's current networking structure and its on-going development. This stage of the research investigated the informal and formal collaborations among the sector actors, and allowed the patterns of sectoral activity of bio-firms, and issues concerning these bio-firms, to be identified in detail.

CHAPTER 5:
A REVIEW OF IRELAND'S ECONOMIC DEVELOPMENT SINCE 1922 AND OF THE EVOLUTION OF THE IRISH GOVERNMENT'S BIOTECHNOLOGY-RELATED POLICIES

5.1 INTRODUCTION

This chapter places the following analyses of the Irish biotechnology sector (bio-sector) in their proper context in relation to Ireland's historical economic development and the development of policies related to the bio-sector. The manner in which policies relating to the development of the Irish economy were/are formulated and implemented depended/depends on the political environment of the time.

This chapter is divided into three sections. The first section presents a general review of Ireland's economic development from independence to the present day, and also of the general industrial policy development trends during the same period. This section highlights how the indigenous economy developed from being a relatively poor, agriculture-based economy towards becoming a highly modern, technology-based economy by the beginning of this century. Section two details the development polices relating to the indigenous bio-sector, particularly policy measures promoting indigenous Science, Technology & Innovation (STI) activities since the late 1950s, specific policies relating to the indigenous bio-sector, and government measures to promote the development of indigenous networks and clusters. The final section discusses how current industrial and STI policies, and the Governments approach towards developing networks and clusters, impacts on current policies in relation to the indigenous bio-sector (a timeline of key events and publications relating to the development of public industrial and science, technology and innovation policies is presented in Figure 5.1).

5.2 IRELAND'S ECONOMIC DEVELOPMENT SINCE THE 1920s

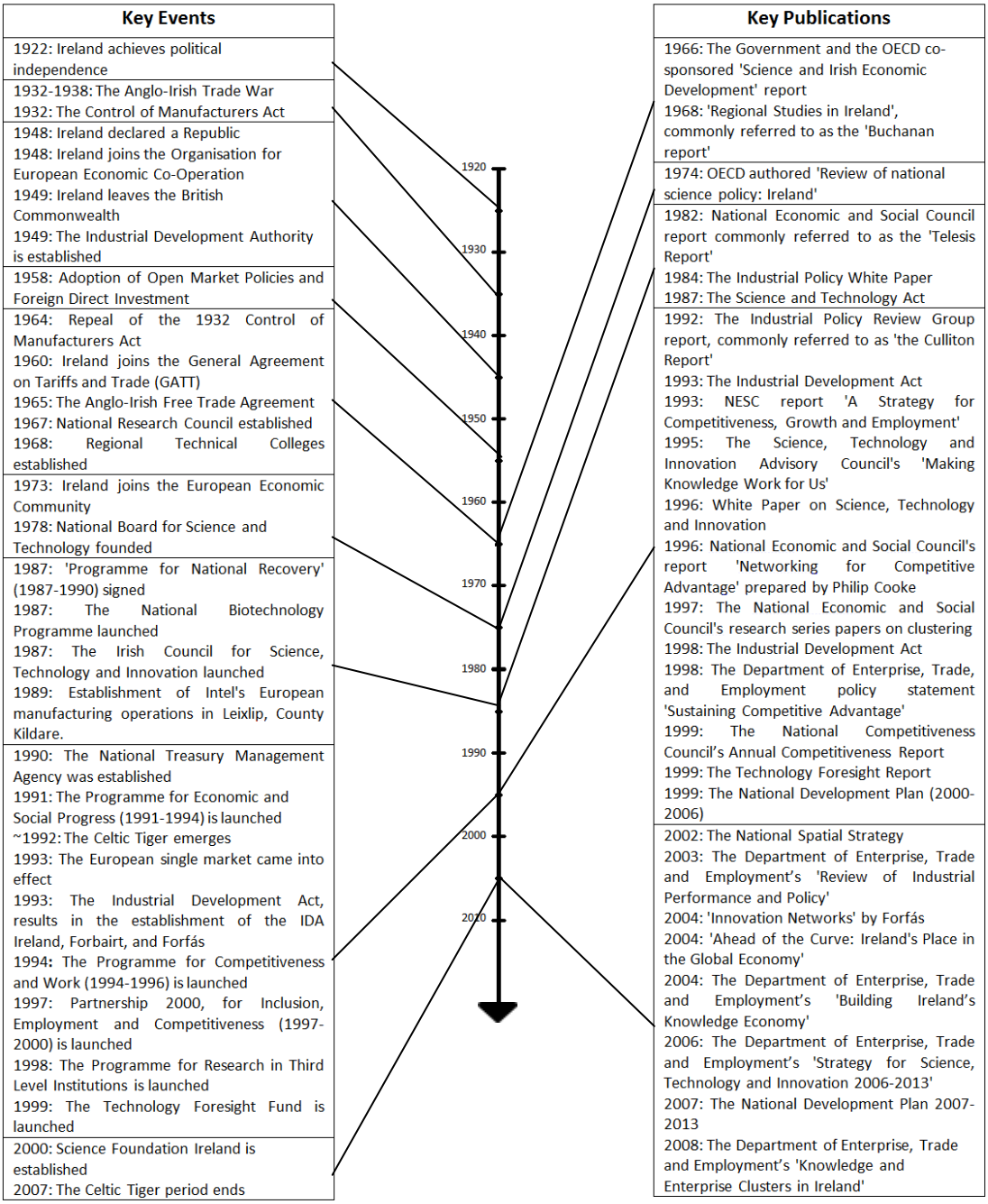
The development of the Irish economy has occurred over a series of stages determined by the political and general economic landscape of the time. This section traces four broad stages in Ireland's economic development: independence and the protectionist era (1922-1957), the open market transformation of the economy (1958-1992), the 'Celtic Tiger' economy (circa 1992-2007), and the post-Celtic Tiger era (post 2007).

5.2.1 Independence and the Protectionist era

In 1922, Ireland achieved political independence from the United Kingdom (UK). The island of Ireland was split into the twenty six counties that subsequently formed the Republic of Ireland, henceforth 'Ireland', and the six counties that make up Northern

Ireland.

Figure 5.1: Timeline of key events and publications relating to the development of public industrial and science, technology and innovation policies.



The country's economy at the time was predominantly centred on agriculture. The 1926 Census of Population showed that 54% of the country's labour force was engaged in agricultural activities, while its industrial base was weak: the country's manufacturing sector comprised 10% of the labour force. The first Irish government, led by William Cosgrave from 1922 to 1932, overwhelmingly focused on the country's agricultural sector, and placed little emphasis on developing the country's industrial base

(Breathnach and Walsh, 1994; Ó Gráda, 1997).

Underlying weaknesses in the country's industrial base could be traced to the 1800 Act of Union between the Kingdoms of Great Britain and Ireland. This effectively created a free trade zone by removing all trade barriers between the two countries. Aside from the Belfast region in the North East of the island, due to its successful linen industry, this caused de-industrialisation in the remainder of the country as it was poorly placed to compete with the highly mechanised industries that had developed in Great Britain during and after the Industrial Revolution (Girvin, 1983; Ó Gráda, 1997).

Essentially, the island was an agricultural centred appendage to the UK economy. This situation remained after political independence, as Ireland remained part of the British Commonwealth until the late 1940s, i.e. the country remained in a free trade area and remained incapable of competing with British industry. The Cosgrave Government's conservative industrial policies advocated free trade, and few economic tariffs were introduced during its rule. Its policy focus on agriculture had very minimal effects on the economy's performance, while the country experienced high emigration rates (Breathnach and Walsh, 1994; Ó Gráda, 1997; Kennedy et al, 1994).

In 1932, political party Fianna Fáil took power, remaining in power until 1948, thus strongly shaping Ireland’s economic direction in this period. Its policy focus was on achieving self-sufficiency in agriculture and industry through protectionist measures and import substitution. This was partly motivated by a balance of trade issue caused by the Great Depression, during which international demand for Irish agriculture products had declined significantly, yet it principally occurred due to a trade dispute with the UK which was subsequently termed 'The Anglo-Irish Trade War' (1932-1938) (Girvin, 1983; Government of Ireland, 2010).

The Trade War began as the new Government refused to continue paying land annuities to the UK Government, i.e. repayments on government loans granted to Irish tenant farmers to purchase lands from their former landlords under the Irish Land Acts (1922) as part of the Anglo-Irish Treaty, also in 1922. The UK Government imposed a 20% tariff on Irish agricultural imports to the UK, which constituted 90% of all Irish exports, and the Irish Government imposed similar tariffs on UK imports into Ireland (Girvin, 1983; Ó Gráda, 1997; Doyle, 1998).

This essentially led to the UK market collapsing for Irish farmers, which dramatically impacted on the agriculture-based economy. In an effort to minimise the Trade War's impact on the industrial sector, the government introduced an import-substitution policy to protect domestic firms through tariffs on imported products, and by encouraging the population to only buy Irish produced goods. To prevent foreign firms establishing Irish subsidiaries to avoid these tariffs, the Control of Manufacturers Act (1932) was introduced to ensure that the majority ownership of Irish companies was limited to Irish citizens. This resulted in 'Capital flight', as potential investors, and British owned firms left Ireland (Girvin, 1983; Ó Gráda, 1997; Doyle, 1998).

The protectionist measures caused a brief surge in industrial-based employment and production, yet the limited sizes of both the Irish market and economy prevented long-term growth. As a result, the Government established many state owned industrial/industrial-related concerns and assumed control of many private concerns, many of these nationalised, state or semi-state owned firms survived until the 1980s/1990s (Abbot, 2001; McHugh, 1984).

The Trade War ended due to political pressures in both the UK and Ireland, yet the Second World War prevented the Irish economy recovering, as general shortages, rationing and disrupted supply routes greatly restricted trade. Ireland benefited from trade with the UK during the World War, during which the Government's protectionist policies were relaxed (Doyle, 1998; Ó Gráda, 1997).

Following the end of the war, Europe underwent a significant and sustained economic expansion period, which ended in the 1970s. Yet, Ireland isolated itself from these developments by fully reinstating and expanding its protectionist policies immediately after the war's end (Ó Gráda, 1997; McHugh, 1984).

Between 1948 and 1957, several changes in Government occurred between Fianna Fail- and Fine Gael-led coalition Governments, in part due to the increasingly poor performance of the economy, including a significant balance of payment issue due to the limited indigenous industrial sector. By the beginning of the 1950s, after almost 20 years of protectionist policies, indigenous manufacturing firms were characterised as being structurally poor. The great majority of firms were small in scale, were engaged in short production runs targeted predominantly for the limited domestic market.

Additionally there was a general lack of specialisation to their activities, while their products were characterised by low quality design and packaging due to their limited R&D and innovative abilities, which were compounded by poor marketing skills. Furthermore, firms "...appeared unwilling or unable to organise production to take advantage of export opportunities during the first post-war decade" (Girvin, 1983: 82).

As a result of the limited industrial sector, substantial imports of industrial equipment and raw materials were required, without any compensating export growth occurring. This resulted in a sustained and significant balance of payments crisis which caused the economy to stagnate, and resulted in a huge increase in emigration: "Net emigration for 1951-6 was 196,763, for 1956-61 it was 212,003. These rates were nearly three times the pre-war rates…" (Lyons, 1979: 625). It was becoming obvious that the protectionist policies were not conducive to long-term industrial growth (Lyons, 1979; Doyle, 1998; Kennedy, 2004).

However, several key decisions were made during this period which had a considerable impact on subsequent economic developments:

- Taoiseach John A. Costello (Fine Gael) declared Ireland a Republic in 1948, and the country left the Commonwealth the following year,
- Ireland joined the Organisation for European Economic Co-Operation, the forerunner of the Organisation for Economic Co-operation and Development (OECD), in 1948,
- the Industrial Development Authority (IDA) was established in 1949 to take responsibility of industrial development, and
- An Córas Tráchtála, the Irish export board, was established in 1952 to aid and assist export-orientated firms (Doyle, 1998; McHugh, 1984; Drew and Foster, 1994; EuroFound, 2009).

5.2.2 Open Market Policies and Foreign Direct Investment

In 1958, the Government, under Seán Lemass (Fianna Fáil), abandoned protectionism in favour of more outward-looking policies. According to McHugh (1984), this change in policy was motivated by the increasingly apparent limitations of protectionism, as well as the counterproductive nature of seeking to industrialise through protectionism.

As stated, protectionist policies had isolated Ireland from the post-war European

economic boom, which was being driven by the increased adoption of open market policies and the development of free trade areas internationally. For example, during the post-war period, the General Agreement on Tariffs and Trade (GATT) (1947), a worldwide agreement to reduce tariffs, and the European Coal and Steel Community (1951), the European Economic Community's (EEC) (1958) forerunner, were established (Collins, 1999; Doyle, 1998; McHugh, 1984).

In order to create an Irish industrial export base, the Government introduced new policies to encourage industrial investment by Irish and foreign companies, through foreign direct investment (FDI), by promoting Ireland's investment potential internationally and through introducing a range of incentives, including:

- the relaxation of the Control of Manufacturers Act (1932) in 1958, and its ultimate repeal in 1964,
- Export Sales Relief, initially introduced in 1956 as a temporary measure to reverse the balance of payments crisis, was expanded to remove corporation tax on profits derived from exports,
- the IDA's activities were augmented to internationally advertise the availability of cheap labour, and
- a range of financial incentives, including substantial capital grants of up to 60% and employment grants (Burke et al, 2003; Cogan and McDevitt, 2000; National Economic and Social Council, 1982; Lyons, 1979; National Economic and Social Council, 1982).

These FDI-orientated policies had a substantial effect. During the 1960s, manufacturing employment levels and exports rose steadily, while the economy grew by an average of 3% a year between 1959-64. However, the indigenous industrial base remained limited as it continued to predominantly focus on serving the Irish market (Clarke, 2006; Collins, 1999).

The open market orientation of the economy was further deepened during the 1960s. Ireland joined the GATT in 1960, and signed the Anglo-Irish Free Trade Agreement with the UK in 1965. A key development during this period was the decision to seek membership of the EEC in 1961. Ireland eventually joined in 1973, meaning it became a cheap location for FDI firms seeking to service the national markets of the enlarged EEC (Clarke, 2006; Kennedy, 2004).

During this period, firms engaging in FDI in Ireland were mainly market-orientated, yet many were attracted by Ireland's low labour costs. At the time, Europe was experiencing a falling unemployment level which was driving up wage levels, thereby making Ireland relatively more attractive as an FDI location. As such, the FDI branch plants which subsequently located in Ireland can be characterised as having involved low skilled, low waged assembly line production to serve the UK and continental European markets, and formed very few local linkages with the economy. This branch plant phenomenon was facilitated by developments in new information and communication technologies (NICTs) and logistics that allowed a TNC's Headquarters to maintain direct control over their overseas operations. By the end of the 1960s, the "attraction of foreign investment now became the primary policy instrument in the contribution to industrial growth" (Girvin, 1983: 83). For example the IDA was reorganised and expanded in 1969, becoming a distinct semi-state body (National Economic and Social Council, 1982).

The Irish economy began to run into problems during the 1970s due to a variety of factors. The global oil crisis in 1973 caused a significant economic shock, resulting in a protracted period of poor economic performance and inflation in most industrialised nations. Additionally, within Ireland there were frequent and protracted official and unofficial disputes "between employers and trade unions and between trade unions themselves" (The Labour Relations Commission, 2000) in key services such as commercial banks and public transport (Rupert, 2004; The Labour Relations Commission, 2000).

During the 1970s, employment declined (between 1973 and 1976, manufacturing employment fell by over 5%), and inflation rates rose. The balance of payments experienced increased pressures due in part to declining agricultural exports, while the Public Sector Borrowing Requirement increased. In efforts to address these issues and the under-performing nature of the economy, the Government introduced various stimulus measures in the late 1970s. Yet, these failed to have much effect due mainly to the impact of the second oil crisis in 1979. Once again, the Irish economy stagnated (McHugh, 1984; Girvin, 1983; Kennedy, 2004; Rupert, 2004).

In 1977, Fianna Fáil returned to Government, and adopted an economic strategy which caused significant economic difficulties during the 1980s. This strategy sought to arrest the high levels of unemployment by expanding the public sector, borrowing heavily to

do so, so as to facilitate a multiplier effect. Yet, interest rates soon increased due to the deepening global financial crisis caused by the oil crisis in 1979, while a 'buy Irish' campaign, introduced to neutralise the impact of the expenditure increase on the balance of payments, failed to have its desired impact. The unemployment rate declined, yet the majority of the newly created jobs were dependent either directly on government spending, or indirectly on deficit finance. This would quickly prove to be unsustainable (Honohan and Walsh, 2002).

5.2.3 The development of 'jobless growth' and steps towards recovery

The 1980s was a turbulent decade for Ireland. The major international recession caused by the second oil crisis strongly affected the country in the late 1970s/early 1980s. The country also experience considerable political turmoil (there were five general elections during the decade, two alone in 1982), while various economic policy decisions unintentionally added to the economic malaise. The late 1970s expansions in public spending ultimately caused the national debt to spiral out of control, from just over €10 billion in 1980 to just over €30 billion in 1987, and resulted in tax rate increases as high as 60% as the various Governments struggled to rein in the worsening economy (Lee, 1989; Doyle, 1998; National Treasury Management Agency, 2000; Honohan and Walsh, 2002).

FDI levels continued to fall, due partly to the high tax rates, as did manufacturing employment, while perversely the output of existing industrial firms increased. This development was termed 'jobless growth', i.e. firms increased productivity through adopting more automated production methods, not through expanding their workforce. It became apparent that the Government's FDI orientated economic policy was increasingly being undermined (National Competitiveness Council, 1998; Girvin, 1983; Honohan and Walsh, 2002).

The Government responded by commissioning a major external review of industrial policy in the form of a National Economic and Social Council (NESC) report in 1982, commonly referred to as the 'Telesis Report' after the American consultancy group which produced it. This report identified several issues that facilitated the emergence of 'jobless growth'. It noted that Ireland's economy was "becoming increasingly dependent on foreign-owned enterprises" (National Economic and Social Council, 1982: 149), and that little development had occurred in the technological or marketing standards of the indigenous industrial sector over the previous two decades. The report stated "no country had succeeded in achieving sustained economic growth except on the basis of

native industry, Telesis queried the Irish emphasis on foreign investment, and advocated greater commitment towards developing an indigenous industrial base" (Lee, 1989: 531; Cogan and McDevitt, 2000; National Economics and Social Council, 1982).

FDI that entered Ireland during the 1970s was mainly in the high-tech sectors of electronics and pharmaceuticals/chemicals, yet their activities remained largely unskilled assembly and packaging work. "Foreign owned industrial operations in Ireland...do not embody the key competitive activities of the businesses in which they participate; [they] do not employ significant numbers of skilled workers..." (National Economics and Social Council, 1982: 151), as automation meant fewer people were required for the low skill activities.

The Telesis report noted that FDI branch plants were not embedded into the Irish economy, stating "...it has to be acknowledged that policy to promote industrial linkages has not lived up to expectations. It is only a mild exaggeration to say that most of the newer foreign firms operate here as essentially an industrial enclave" (Industrial Policy Review Group, 1993: 31). Linkages to the economy were very limited as the plants made little use of Irish suppliers, and had no marketing or R&D facilities. The report noted little effort had been made to attract such aspects into Ireland to embed FDI, and that Ireland had to become more selective in the types of FDI it was attracting, by focusing on higher skilled activities and firms who would require extensive local sub-suppliers (National Economic and Social Council, 1982; Cogan and McDevitt, 2000).
Ireland was seen as a "...convenient manufacturing satellite for sales in the EEC. Over 80% of the companies visited during our study came to Ireland primarily because it provided a tax shelter for penetrating the EEC" (National Economics and Social Council, 1982: 135). Ultimately, the foreign branch plants were profit generators, with the profits being repatriated back to the firms' headquarters (The United Nations University, 1994).

The report also noted indigenous firms were poorly developed and had "...not succeeded in developing competitive positions from new product ideas" (National Economic and Social Council, 1982: 127). The report characterised Irish business as being stunted due to decades of protectionism and limited political interest in developing indigenous industry. It also commented that "a native entrepreneurial cadre of the requisite quality had failed to emerge. Irish-owned industry could not compete internationally. It could

not even compete in the home market" (Lee, 1989: 536). The report called for a reduced dependence on FDI and an enhanced role for domestic industry, mainly through tackling the marketing and management defects which were a feature of the domestic sector (Industrial Policy Review Group, 1992).

The Government responded to the Telesis report's findings and recommendations with the Industrial Policy White Paper in 1984. However, the Telesis report's main recommendations were largely ignored, as no major shift in focus occurred towards indigenous industry. The Government did introduce a Technology Acquisitions Grants Scheme and a National Linkage Programme to improve linkages between foreign branch plants and indigenous firms, yet both programmes met with limited success. The issues identified by the Telesis Report essentially remained (Cogan and McDevitt, 2000; Industrial Policy Review Group, 1992).

The economic malaise continued through the decade, e.g. the National Debt as a percentage of Gross Domestic Product (GDP) had risen from almost 90% of GDP in 1982 to almost 130% of GDP in 1986, while unemployment increased from 7.1 per cent in 1979 to almost 18 per cent in 1987. Drastic economic measures arrested the declining state of the country's finances by the mid 1980s, yet failed to lead to a noticeable recovery (O'Donnel and O'Reardon, 1996; Honohan and Walsh, 2002).

In 1987, the Fianna Fail Government, with active support from the main opposition party, implemented an extensive series of economic reforms which facilitated a relatively modest recovery towards the end of the decade. These measures included tax cuts, a dramatic reduction in Government spending, and a temporary freeze on public sector recruitment in combination with cutbacks in public capital spending (National Treasury Management Agency, 2000; Honohan and Walsh, 2002).

Several important developments occurred in the late 1980s which subsequently had significant impacts on the economy. In 1987, the first Social Partnership agreement, the 'Programme for National Recovery' (1987-1990) was signed. This was a voluntary, socially oriented economic agreement between the Government, employers groups and Trade Unions that aimed to increase national competitiveness through strike and wage moderation, in return for tax reforms and action on unemployment. Also in 1987, the International Financial Services Centre (IFSC) was established in the Dublin's

docklands. This offered a range of tax and other incentives to financial services firms that established operations within its defined zone (O'Donnel and O'Reardon, 1996; National Treasury Management Agency, 2000; Honohan and Walsh, 2002; Goodbody Economic Consultants, 2007; White, 2005).

However, one of the most important developments for the economy occurred in 1989 with the establishment of Intel's European manufacturing operations in Leixlip, County Kildare. This development changed the industrial base of Ireland's economy by attracting more complex FDI investments in this field into Ireland through signalling "the availability of a well-educated workforce, attractive taxation and incentives, the availability of suitable land, good infrastructure services...[and] the quality of life in Ireland" (Keith Thompson, Intel vice president, quoted in Lillington, 2009; IDA Ireland, 2010; Coleman, 2000).

Additionally, the country benefited from the receipt of expanded EU structural grants after 1988. These grants, particularly those received under the European Regional Development Fund, had a substantial impact through allowing the government to complete infrastructure projects which had been deferred during the 1980s, without undermining the economy's initial recovery (Honohan and Walsh, 2002; Acheson, and Lambkin, 2009; European Commission, 2009).

5.2.4 The 'Celtic Tiger' era

Unlike the 1980s, the political climate during the 1990s was more stable. The main political focus was on continuing the economic recovery initiated in the late 1980s. During the early 1990s, several developments had a massive impact on the economy:

- the National Treasury Management Agency (NTMA) was established by the Government in 1990 to manage the National Debt,
- the national pay agreement continued with the Programme for Economic and Social Progress (1991-1994), and
- the European single market came into effect in 1993, facilitating free movement of goods and services, labour and capital between EU member countries. This had a massive impact on Ireland's ability to attract FDI (Cassidy and O'Brien, 2005; National Treasury Management Agency, 2000).

In an attempt to optimise the future performance of the economy, the Government

sponsored another report to review the country's industrial policy, the Industrial Policy Review Group (1992), commonly referred to as 'the Culliton Report' after its chairman. This report reiterated many of the Telesis Report's findings, i.e. that while FDI had made enormous contributions to the Irish economy over several decades, "...the attraction of foreign investment is not a sufficient basis for developing a national advantage in advanced industries...Industrial growth through dependent branch plants of foreign firms can get us only so far" (Industrial Policy Review Group, 1992: 66).

The report called for the country's industrial policy focus to shift away from FDI, i.e. that future industrial development should be based on cultivating and developing indigenous industry, as there was a pressing need "...to have more firms that are Irish managed, have growth potential and are better integrated into the economy than the typical dependent branch plant of a foreign multinational" (Industrial Policy Review Group, 1992: 66). The report detailed a variety of key policy recommendations, including greater investment in R&D and a radical upgrading of the technological competence of indigenous industry (Breathnach, 2001; Cogan and McDevitt, 2000).

The Government responded to many, but not all of the report's recommendations under the 1993 Industrial Development Act. EOLAS and the IDA were dissolved and three agencies were established:

- IDA Ireland: to focus solely on attracting FDI through selectively targeting sectors with long-term development potential and whose activities putatively would mean branch plants would have to develop linkages with the local economy,
- Forbairt: EOLAS was subsumed into Forbairt, which focused exclusively on indigenous enterprise development, and
- Forfás: which was created with responsibility for overall industrial policy formulation and to coordinate the work of Forbairt and the IDA Ireland (Burke at al, 2003; Breznitz, 2007; Government of Ireland, 1993a, 1993b).

No serious efforts were made to move economic policy away from FDI, despite the Culliton report's findings. Yet, the Irish economy's subsequent transformation, due to the emergence of the Celtic Tiger economy in the early 1990s, effectively pushed indigenous sectoral development issues aside (van Egeraat and Breathnach, 2006).

During the Celtic Tiger economy (circa 1992~2007), Ireland was transformed into a post-industrial economy in a relatively short period of time. The country's GDP almost doubled in real terms between 1992 and 2001, while average living standards rose dramatically, and per capita GNP moved from around sixty percent of the EU average in the late 1980s to almost one hundred percent by 2001 (Cronin, 2005; Breathnach, 1998; Honohan and Walsh, 2002).

The exact causes for its emergence are debatable, yet one of the main forces behind the Celtic Tiger was a surge of inward investment that followed Intel's decision to locate its European manufacturing operations in the country in the late 1980s. This new FDI was attracted to Ireland due, in part, to the stability of the social partnership agreements, and decades of investment in higher education (in combination with a baby boom in the 1970s) which resulted in a highly skilled and relatively cheap labour force. Additional factors included the continuing low rate of corporation tax, and Ireland's membership of the EU (Breathnach, 2001; Honohan and Walsh, 2002; van Egeraat and O'Byrne, 2010).

These new investments were in modern 'high-tech' sectors, such as the electrical and optical equipment sector and the capital-intensive pharmaceuticals sector, that involved more high skilled activities and more sophisticated manufacturing production processes than the activities which had typified FDI since the early 1960s. As such, a significant shift in the composition of the manufacturing sector occurred, with a corresponding surge in manufacturing employment (Breathnach, 1998; Honohan and Walsh, 2002).

Record job creation levels occurred in both foreign and indigenous companies. At a sectoral level, the services sector (particularly financial, business, health, and education services) accounted for the largest proportion of employment generated, while many 'low-tech' low skilled manufacturing activities and jobs were replaced by high-skilled, high wage jobs, most notably in NICTs and Pharmaceuticals (Cronin, 2005; Goodbody Economic Consultants, 2007; Honohan and Walsh, 2002; van Egeraat and O'Byrne, 2010).

Even as the Celtic Tiger emerged, following the recommendations of the Culliton report, the Government commissioned a report by the Science, Technology and Innovation Advisory Council (STIAC) (established in 1994) to review the country's

Science, Technology and Innovation policy. The report, 'Making Knowledge Work for Us' (1995) (the report's findings are discussed further in the following section), highlighted the continuing lack of embeddedness of FDI branch plants, and the continuing small size, scale, and R&D levels of indigenous industry (Forfás, 1996; Acheson, and Lambkin, 2009).

The government established a task force to implement the report's recommendations. This led to the country's first ever White Paper on Science, Technology and Innovation in 1996 (discussed further in the following section). The most important outcome of the White Paper was the Industrial Development Act (1998), which merged the Irish Trade Board (which marketed Irish goods and services nationally and internationally) and Forbairt to form Enterprise Ireland (EI), i.e. one main government agency was now, and remains, solely responsible for indigenous industrial development (Burke et al, 2003; OST 1996; Acheson, and Lambkin, 2009).

As the 1990s progressed, the Celtic Tiger's impact on the economy deepened. Increased prosperity and low interest rates in the mid 1990s, resulting from the departure of Sterling from the European Exchange Rate Mechanism in 1992, led to significant private investments in the housing sector. Significant infrastructural development occurred through EU Structural Fund investments, e.g. the country's motorway network expanded significantly. In 1995, the Free Fees Initiative drastically reduced the costs of under-graduate third level education, furthering the country's skilled labour supply. Additionally, the National Pay Agreements continued with the Programme for Competitiveness and Work (1994-1996), and the Partnership 2000, for Inclusion, Employment and Competitiveness (1997-2000) (Honohan and Walsh, 2002; EuroFound, 2009; International Labour Organization, 2003).

Yet, at the beginning of the new millennium “the [Irish] economy was displaying unmistakable signs of overheating” (Honohan and Walsh, 2002: 11). According to Cassidy and O'Brien (2005), the country's reliance on FDI had created significant weaknesses, as demonstrated through the substantial slow down in Ireland’s export growth after 2000 which was caused by several shocks to the Irish and global economy in 2001. The Irish economy's competitiveness was being undermined by its rising cost base, e.g. a steady increase in consumer prices, while a global downturn in the NICT sector had a severe impact on the Irish economy due to the country's high export

specialisation in the sector (Cassidy and O'Brien, 2005).

While indigenous industry had expanded during the Celtic Tiger era, indigenous sectors remained in much weaker competitiveness positions, and continued to be characterised as being more traditional, labour-intensive, less research intensive and more embedded in the domestic economy than the high-technology FDI sectors. The structural weaknesses of indigenous industry were now spread "across numerous dimensions, suggesting that the [indigenous] sector would find it almost impossible to ramp up sufficiently rapidly to be able to replace foreign industry in the event of a sharp adverse shock to the latter" (Barry, 2006: 41). Essentially, the economy was now vulnerable to external shocks, such as "a significant downturn in the US economy" (Cassidy and O'Brien, 2005: 75).

The early 2000s also saw a significant fall in manufacturing employment as more routine, labour-intensive activities relocated overseas, especially to China and Eastern Europe, e.g. clothing manufacturer Fruit of the Loom closed its Irish-based operations in 2004. Export growth recovered in 2004, due in part to the introduction of the Euro in 2002, which further reduced inter-EU transaction costs and stimulated export growth, yet also due to a recovery in the global NICT sector. Additionally, several major new TNC investments occurred, e.g. Google opened its European HQ in Dublin in 2004. The economy's growth continued due to a construction boom and a strong growth in services exports, yet not at the level of the mid-to-late 1990s (van Egeraat and Breathnach, 2006; Lavery, 2004; IDA Ireland, 2009).

However, at this point serious competitiveness issues were apparent in the economy. Many senior economists, nationally and internationally, commented that while Ireland's economic growth was strong, e.g. government debt had been reduced dramatically and the unemployment rate was low (due to rising labour participation rates), the economic recovery was mainly being driven by the indigenous construction industry and significant increases in property values, e.g. national house prices increased by 270% between 1996 and 2006. Economic growth had become unbalanced due to the reliance on the construction industry. By 2006, almost 20% of Ireland's private sector workforce employment was dependent, directly or indirectly, on the property sector (Hennigan, 2006; The Irish Times, 2003; Goodbody Economic Consultants, 2007).

Additional issues included “a sudden and substantial acceleration in the rate of consumer price inflation” (Cassidy and O'Brien, 2005: 85) following the Euro's introduction, and a steep rise in the total level of private sector debt due to investments in the property market. The Organisation for Economic Co-operation and Development (OECD) and senior Irish officials of the Central Bank and Financial Services Authority of Ireland noted that the Irish property market was overvalued by 15% in 2005. By April 2006, officials in the Irish Central Bank commented that the housing boom displayed significant signs of instability and posed a 'significant risk' to the economy (Murphy et al, 2008; Brennan, 2007; Lillington, 2009; Hennigan, 2006; The Irish Times, 2005; Goodbody Economic Consultants, 2007).

Ireland, in particular the Greater Dublin Area (GDA), where the majority of the economic activity derived from the Celtic Tiger was focused, was increasingly expensive as a place to do business and to live, for a variety of reasons. Wage costs, particularly in the GDA, began to rise sharply. Two international surveys ranked Dublin within the top ten most expensive cities, globally, for office occupancy costs. The GDA's success also led to an unbalanced pattern of economic and spatial development at a national scale, as reflected in Ireland losing its Objective 1 status with the EU's structural funds. After 2000 the Country was divided into the Southern and Eastern areas (Objective 2) and the Border, Midland and West area (Objective 1) (Power, 2007; European Commission, 2000; van Egeraat and O'Byrne, 2010).

Additional factors undermining Ireland's competitiveness included the increase in the corporation tax rate applied to manufacturing and certain internationally traded services from 10% to 12.5% in 2003 due to pressure from other EU members. Ireland faced increased competition from countries offering low taxes, cheap land prices, and educated workforces in efforts to attract FDI. Indeed, by the late 2000s, one of Intel's former Presidents commented that only one of the list of reasons why Intel had come to Ireland in 1989 still held, i.e. tax benefits (Lillington, 2009). The increased competition for FDI, and the decreasing national competitiveness was ultimately reflected in the decision of several large FDI firms to relocate Irish operations to such locations, e.g. the closure and relocation of Dell's Limerick-based manufacturing to Poland in 2009 (Lillington, 2009; Mellor, 2009; Goodbody Economic Consultants, 2007; Honohan and Walsh, 2002).

By the beginning of 2008, it was apparent the Celtic Tiger era was ending. The country's property bubble began deflating in 2007, leading to a downturn in the construction dependant economy. This downturn was subsequently magnified by the impact of the global financial crisis, caused by massive liquidity issues (the 'credit crisis') in the US banking system that first appeared in 2007, and which subsequently sparked a global recession (Clark, 2008; Hennigan, 2006).

5.2.5 The post 'Celtic Tiger' economy

This global recession had a massive initial impact on the Irish economy. Unemployment as a percentage of the Labour force rose from 4.5% in 2007 to 13.2% in 2009. During the same period the general Government debt as a percentage of GDP rose from 24.8% to 57.7%. Contractions in GDP during the first half of 2008 indicated that the Irish economy had entered its first recession since the 1980s (Davy Research, 2009; Barret et al., 2009**;** FinFacts, 2009b).

An emergency budget was introduced in July 2008 in an effort to halt the declining state of the public finances, which introduced drastic budget cuts. However, these measures proved unsatisfactory and a supplementary budget was introduced in April of 2009 to address a revenue shortfall caused by rapidly declining tax revenues of close to €4.5 billion. Funding to many Government policies and initiatives was cut back or withdrawn in an effort to address the poor state of the economy (Doyle, 2009; Davy Research, 2009; Barret et al., 2009**;** FinFacts, 2009b).

The Irish banking sector, which had become over-exposed to the Irish property market during the property bubble, came under severe pressure in the second half of 2008, as house and land prices continued to decline. The government was forced to nationalise the country's third largest bank, Anglo Irish Bank, and to recapitalise its top two banks, the AIB and the Bank of Ireland. In an attempt to address the worsening liquidity issues of the banks, the Government proposed a National Asset Management Agency (NAMA) in April 2009 to take over large property-related loans from the banks, to enable them to return to normal liquidity to assist in the economic recovery (Doyle, 2009; FinFacts, 2009a).

At present the Irish economy shows tentative signs of recovery, yet the long-term effects of the post-Celtic Tiger economic slump are difficult to predict. The ESRI (Fitzgerald et

al., 2008) predicted the current economic contraction of the Irish economy will level off around 2012-2014, with the economy expected to recover to near-2007 levels by 2020, yet it must be noted these predictions were formulated without considering the future impact of NAMA on the economy. The strong growth experienced during the Celtic Tiger is ultimately expected to give way to more sustainable increases over the next decade, with GDP and GNP growth averaging around 3 per cent between 2010 and 2020 (Fitzgerald et al., 2008; Indecon International Economic Consultants, 2008; van Egeraat and O'Byrne, 2010).

The ESRI also projects the trend of declining FDI in 'traditional' manufacturing activities to continue due to increasing international competition and the decline in Ireland's competitiveness for such activities. In relation to future employment trends, growth is likely to be heavily concentrated in the services sector, including the internationally traded and domestic services activities, with particularly strong growth in market services employment (Fitzgerald et al., 2008; Indecon International Economic Consultants, 2008; van Egeraat and O'Byrne, 2010).

5.3 THE DEVELOPMENT OF GOVERNMENT POLICIES RELATING TO BIOTECHNOLOGY

5.3.1 Measures to promote Science, Technology & Innovation, and the indigenous bio-sector

From independence up until the late 1950s, the predominant focus of the various Irish Governments' Science, Technology and Innovation (STI) and industrial policies was towards the country's agricultural and food sectors. This contributed to, and compounded the negligible role innovative research played in indigenous industry; as detailed in the previous section, industry at the time was characterised as engaging in limited research activities, there had been little need to innovate due to decades of tariff protection (Acheson, and Lambkin, 2009; Teavey, 1995).

The development of Irish STI policy began in earnest in the 1960s. In 1963, the Government and the OECD co-sponsored the 'Research and Technology Survey' to assess Irish scientific and technological research activities in order to inform the formulation of research-related and economic-orientated policy recommendations. The ensuing report, Science and Irish Economic Development (1966), highlighted Ireland’s need to actively develop science and technology in order to drive economic development. The Government responded to the report's main recommendation through establishing a National Research Council in 1967. The council's main responsibilities

were to advise the Government on policies related to industry and research, the development of a national research programme, and the establishment of the Regional Technical Colleges in 1968. The Council also provided a very limited number of annual research grants (Murphy, 1972; OECD, 1966; Acheson, and Lambkin, 2009).

Cooper and Whelan (1973) noted that despite the changes to the Government's approach to research, the country's Public Research and Education Organisations (PREOs) research activities remained predominantly focused on agriculture, with little attention being paid towards industry. Additionally, due to their low level of research activities, indigenous firms could not benefit from these increased R&D activities, i.e. an innovation paradox existed, while the relatively more high-tech FDI firms had no interest in Irish R&D activities due to their branch-plant orientation (Cooper and Whelan, 1973; Teavey, 1995).

These comments were repeated in the 1974 OECD review of the Irish government's science policy, 'Review of national science policy: Ireland'. This review noted that the existing science policy lacked co-ordination, that R&D activities outside of state sponsored programmes remained minimal. It recommended the establishment of a Government agency to implement a coordinated science policy. In 1978, the Government responded by establishing the National Board for Science and Technology (NBST), which sought to place research policy at the centre of economic development, and established a limited grants scheme for the development of scientific and technological research (Government of Ireland, 1977; OECD, 1974; Yearley, 1995; Acheson, and Lambkin, 2009).

Following the emergence of the biotechnology industry in the mid-1970s, governments in developed economies, and supra-national agencies, such as the European Economic Community (EEC), were quick to respond to the industry's economic possibilities. The Irish Government noted biotechnology's potential importance for Ireland's future economic development at the time, yet was relatively slow in developing policies to encourage/facilitate the development of indigenous capabilities in this area (Burke et al, 2003; Kennedy et al., 1994).

It must be noted that many of the Irish Government STI-related initiatives, and biotechnology-related initiatives which developed from the late 1970s onwards were

supported and/or motivated by a variety of EEC/European Union (EU) programmes, particularly through the different Framework Programmes (FPs). Since the first FP in 1984 (the current, seventh, FP runs until 2013), the EU has viewed the life sciences/biotechnology as being one of the key technology areas of the 21st century, particularly in relation to health care, agriculture, environmental protection, energy production and industrial processes. The importance of the FPs for Ireland's STI efforts increased during the 1980s, as public funding to STI-related agencies and policy initiatives suffered significant cuts as the various Governments tried to stabilise the declining economy, as detailed above (Pownall, 2000; Urwin, 2001; Cordis, 2006; Yearley, 1995).

One of the first measures designed specifically to promote biotechnology in Ireland was established in 1983 by the NBST as part of an effort to compile a coordinated national STI programme. The Programme for Strategic Research provided grants for research in selected niche areas including biotechnology, NICTs and engineering. However, the programme's impact was limited as its total grant funding amount was "considerably less than £1 million" (Yearley, 1995: 187) a year (Kennedy et al., 1994; Downey, 1979; Senker and Van Zwanenberg, 2000).

Due to the rapid emergence and increasing impact of biotechnology internationally, the NBST and the IDA began investigating how establishing biotechnology-related expertise in Ireland could contribute to economic growth and productivity. In 1984, a model was devised for a National Biotechnology Initiative, which proposed the establishment of four centres based on three areas:

- traditional processes, e.g. brewing and cheese making,
- modern fermentation industries, e.g. enzymes and antibiotics, and
- new industries resulting from biotechnology technologies, such as recombinant DNA (Burke et al, 2003; Kennedy et al., 1994; Office of the Houses of the Oireachtas, 2004).

In 1987, partly motivated by the EU FPs, the government published the Science and Technology Act, shifting its science policy away from FDI towards promoting industrial development through the use of science and technology. The Act led to significant institutional reforms, including the creation of an Office of Science and Technology within the then Department of Industry and Commerce (presently the Department of

Enterprise, Trade and Innovation) and the formation of a unified agency, EOLAS, through the merger of the NBST and the Institute for Industrial Research and Standards (which had been responsible for setting and monitoring technical standards in industry). EOLAS was charged with developing a national programme in science and technology, and the development of closer linkages between PREOs and indigenous firms, so as to address the firms' limited innovative capacities. A key development, relating to STI policy, was the shift away from fixed asset investments and direct grants towards seeking to develop people, skills, and research capabilities (Burke et al, 2003; Cogan and McDevitt, 2000; Acheson, and Lambkin, 2009; National Economic and Social Council, 1993).

The National Biotechnology Programme (NBP) was launched in 1987 as part of the Science and Technology Act, and introduced cooperative activities to commercialise PREO-based research through developing links between PREO researchers and the bio-sector, and through the formation of start-up companies. The NBP's model differed from the proposed National Biotechnology Initiative in that five research institutes (RIs) were established in five different PREOs (as detailed in Appendix D). Each RI operated independently from the departmental structure of their host universities, and had its own specific research focus. In 1988, the NBP was renamed BioResearch Ireland (Burke et al, 2003; Cogan and McDevitt, 2000; The ELS Gazette, 2002).

By the end of the 1980s, the level of Government funding available to the Irish scientific community remained limited, e.g. in 1990, “EOLAS's scientific program was intending to make around twenty awards averaging £15,000; little scientific apparatus could be purchased for such sums” (Yearley, 1995: 190). The majority of funding for scientists continued to come from the various EU initiatives under the FPs.

As stated previously, the Government established the STIAC in 1994 following recommendations from the Culliton Report (1992) to formulate policy proposals on Science & Technology. The following year, STIAC published its report, 'Making Knowledge Work for Us' (1995), which highlighted the limited Governmental support for PREO-based basic and applied research activities. The Travers Task Force (chaired by John Travers, then Chief Executive of Forfás) was established to suggest ways to implement the report's recommendations. This led to basic research grants increasing from £1 million to £1.5 million (€1.27 million to €1.91 million, respectively), with an

extra £4 million (just over €5 million) being allocated to the country's total science research budget. An STI awareness programme was also launched, and grants to fund Ph.D. and post-doctoral programmes in biotechnology/biotechnology-related subjects were increased (Burke et al, 2003; Forfás, 1995, 1996; Science and Technology Division, 1995; Acheson, and Lambkin, 2009).

The Government responded to the STIAC report in 1996 with the country's first White Paper on Science, Technology and Innovation. This argued that indigenous industry needed to move away from traditional manufacturing activities towards a knowledge and know-how based economy, and recommended increasing their R&D and innovation abilities through the implementation of a coherent Science, Technology and Innovation (STI) policy, and the provision of greater resources for knowledge generation activities in the country's PREOs (Cogan and McDevitt, 2000; Cooke, 1996; Acheson, and Lambkin, 2009).

The White Paper led to the creation of the Irish Council for Science, Technology and Innovation (ICSTI), the establishment of an interdepartmental committee, and a cabinet sub-committee on Science & Technology. Additionally, the Office of Science and Technology, within the Department of Enterprise, Trade and Employment, now formulated and developed all STI-related policies across all Government Departments (Burke et al, 2003; Acheson, and Lambkin, 2009).

A significant surge in STI and biotechnology-related initiatives followed in the wake of the White Paper. An additional boost to Ireland's scientific research capacity occurred when the Higher Education Authority (HEA), the statutory planning and development body for higher educational and research in Ireland, established the Programme for Research in Third Level Institutions (PRTLI) in 1998 to assist the "...development of [third level] institutional research capabilities through investments in infrastructure and in research programmes and support high-quality interdisciplinary and inter-institutional research" (Higher Education Authority, 2006: 11) (the HEA and PRTLI are detailed further in chapter 6) (Ryan, 2004; Higher Education Authority, 2005, 2006).

Also following the White Paper's recommendations, the Government commissioned a Technology Foresight exercise in 1998. The subsequent Technology Foresight Report (1999) concluded that NICTs and biotechnology were "two pervasive and strategic

technologies underpinning many existing sectors in the economy and likely to underpin 'new' industries in the future" (Acheson, and Lambkin, 2009: 8). The report recommended the establishment of a research fund to invest in niche technology areas, such as biotechnology, in order to enhance and ensure Ireland's future competitiveness, while it stated that investments in STI-related infrastructure were required to establish an internationally competitive PREO research base and stimulate the creation of PREO derived indigenous technology-based firms (Irish Council for Science Technology and Innovation, 1999; Acheson, and Lambkin, 2009).

A major advancement in STI policy occurred with the launch of the National Development Plan (NDP) (2000-2006) in 1999, which allocated €2.5 billion specifically for research, technology & innovation activities through the Research, Technological Development and Innovation (RTDI) fund. This fund had several objectives:

- to strengthen the research capacity of Irish PREOs and other research establishments relevant to the needs of the Irish economy,
- to strengthen the capacity of Irish firms to assimilate the results of R&D into their products and processes, and
- to provide support for sectoral research in agriculture, food, marine and the environment (National Development Plan, 2005a, 2005b: Forfás, 2003; Burk et al, 2003).

As part of the NDP, following the Technology Foresight Report's recommendations, the government created ` (TFF) in 1999 to facilitate the development of PREO research in NICTs and biotechnology. The following year Science Foundation Ireland (SFI) was established as a sub-board of Forfás to administer and manage the TFF (Burke et al, 2003; Department of Trade, Enterprise and Employment, 2000: 2001; ERCIM News, 2000; Acheson, and Lambkin, 2009).

These initiatives represented the first introduction of long-term, strategic approaches towards the development and funding of indigenous STI capacity in the State's history. By 2004, the R&D expenditure of the PREOs had reached almost €500 million, predominantly due to the PRTLI and the TFF (Forfás, 2005a, 2005b; Acheson and Lambkin, 2009).

The Government subsequently committed to continuing and developing these initiatives

through the National Development Plan 2007-2013 (2007), which includes a provision for a €20 billion investment in Enterprise, Science and Innovation, with €8.2 billion being specifically allocated for scientific research. SFI has been charged with the responsibility of investing €1.4 billion, focused again equally on NICTs and biotechnology, while the PRTLI has been extended with €190m being provided for the programmes fourth cycle over the period 2007-2010 (Science Foundation Ireland, 2007; The Higher Education Authority, 2007a, b).

These on-going programmes and initiatives have moved beyond primarily focusing on building infrastructure and developing a critical mass in PREOs towards developing optimal conditions conducive to the creation of commercial concerns from PREO-based research (Department of Trade, Enterprise and Employment, 2006; Government of Ireland, 2007).

The Government announced a new Strategy for Science, Technology and Innovation (2006-2013) in 2006. This acknowledged that STI remained relatively underdeveloped in Ireland in relation to international standards, particularly in the transfer of PREO-based research to the market place. The strategy aimed to facilitate the development of integrated science courses from primary level education to the fourth level, addressing research-related structural weaknesses in the country's PREOs (through the NDP), by developing the necessary soft and hard support structures to facilitate rapid technology transfers from PREOs, and also addressing the limited R&D capabilities and activities of indigenous firms (Acheson and Lambkin, 2009; Forfás, 2008).

The strategy aims to develop industry-led research activities through the development of competence centres that translate firm-based research into commercialisable technology through collaborative research activities with PREO researchers. Jointly run by EI and the IDA Ireland, nine centres will ultimately be formed (none of which will be overtly related to the indigenous bio-sector) as collaborative translational research-based activities. A PREO/Small to Medium Enterprise (SME) collaborative initiative has recently been introduced by the Department of Enterprise, Trade and Innovation as part of the strategy, i.e. 'Innovation Vouchers' (Forfás, 2006, 2008; Acheson and Lambkin, 2009; Department of Enterprise, Trade and Employment, 2008; Forfás, 2008).

5.3.2 Government measures to promote indigenous networks and clusters

One of the first mentions of networks in Irish Government literature occurred in the

Industrial Policy White Paper in 1984. The Government subsequently introduced a Technology Acquisitions Grants Scheme and a National Linkage Programme to improve linkages between the FDI branch plants and indigenous firms. However, both programmes had limited success due to the limited research capabilities of indigenous firms and the outward focus of the FDI branch plants (as detailed previously) (Cogan and McDevitt, 2000; Industrial Policy Review Group, 1992).

Due to the perilous state of the nation's economy during the 1980s, successive governments focused almost exclusively on addressing the dire state of the nation's finances at the expense of other policy areas. Topics such as networking were relegated to positions of low importance.

Networks next appeared in the 'Culliton Report' in 1992. A key recommendation of the report was the promotion of industrial clusters of interlinked firms built around pre-existing local strengths. Additionally, it proposed that the indigenous development agency (then EOLAS) should be organised on regional lines to be more conducive to cluster promotion. Yet, with the publication of the 1993 Industrial Development Act, the Government avoided committing to developing clusters, and opted to organise Forbairt (which subsumed EOLAS) on a sectoral basis for unstated reasons (Burke at al, 2003; Breathnach, 2001; Cogan and McDevitt, 2000).

The Culliton Report's clustering recommendations were subsequently supported by the publication of the NESC report 'A Strategy for Competitiveness, Growth and Employment' in 1993. This recommended the introduction of SME supports in areas such as innovation and management due to the increasing impact of Post-Fordism internationally, along with parallel co-operative structures to promote networks of related firms. However, the report also concluded that introducing such policies would prove problematic as they would require a level of vision and organisational capacity likely to be beyond the capabilities of the state sector (Breathnach, 2001; National Economic and Social Council, 1993).

Following the publication of the STIAC report in 1996, the Government published the White Paper on Science, Technology and Innovation. This argued that Irish industry needed to move away from traditional manufacturing activities towards a knowledge- and know-how based economy. It recommended that the basic structural issue of Irish

firms, e.g. their small size and scale and low levels of R&D, be addressed through cultivating co-operating groups of companies through an Inter-Firm Cooperation Programme where firms would collaborate in key areas such as "...R&D, technology acquisition, process change and market development" (STIAC, 1995: 70), i.e. a network-based programme. The STIAC report recommended a brokerage service be implemented to facilitate network developments and information sharing among indigenous firms, similar to the Danish network programme detailed in chapter 2 (Cogan and McDevitt, 2000; Cooke, 1996).

The Government's response to the report's proposals was generally positive. A steering group was set up in the Office for Science and Technology to investigate its findings. A consultancy report prepared in 1996 to analyse nine inter-firm networks between SMEs concluded that networks allowed firms to achieve greater economies of scale than when they were independently-operating entities. The report also found that where firms were located in close geographic proximity, the benefits of the networks were enhanced (Breathnach, 2001, Forfás, 1994; Engel and Del-Palacio, 2011).

Also following the STIAC report, the NESC published two reports relating to networks and clustering. The first report, prepared by Philip Cooke (1996), looked at inter-firm networking in Europe, while the second (1997) was comprised of three studies in a research series that looked at clustering in three successful indigenous sectors (ADAPT, 2002).

Cooke's report again highlighted the serious issues present in Ireland's manufacturing sector, i.e. a strong FDI sector existed, yet one with few indigenous linkages, while indigenous firms remained predominantly small in size, had limited innovation capacities and had limited opportunities to learn from external sources, including PREOs. Cooke felt that the optimal way to develop indigenous firms was through establishing industrial clusters. He noted that in certain industrial areas in Europe, such as Baden-Württemburg in Germany and the Emilia-Romagna region in Northern Italy, a strong networking culture existed which heavily promoted innovation: "Industrial clusters are also a key feature of successful European economies…these are vertically and horizontally linked supply and subcontracting chains in interaction with public and private enterprise support services" (Cooke, 1996: vii).

Cooke identified two main learning methods in his study, i.e. firm interaction (linkages and/or joint R&D initiatives) and learning from R&D conducted elsewhere, often conducted by a group of collaborating firms analysing and disseminating information on their competitors. Both methods involved inter-firm networking. Cooke recommended that co-operative structures should be established among Irish firms to achieve some of the economies of scale available to large firms: "…enterprise support for wider cluster formation should be provided to link...'networks of networks' around areas of major economic strength such as food, pharmaceuticals and electronics" (Cooke, 1996: vii). The proposals rationale was that government support in the areas of innovation and management would be less effective for individual firms unless this support was accompanied by measures promoting networks of related firms at sectoral and regional level (Breathnach, 2001).

Cooke recommended institutionalising an interactive innovation culture through the establishment of a network programme derived from the Danish Network Cooperation Programme. This recommendation echoed the STIAC's network strategy proposal by seeking to assist the creation of inter-firm networks through a broker service. Cooke also proposed the subsequent establishment of a Cluster Support Programme to facilitate the development of clusters.

Following the publication of Cooke's report, Forbairt initiated a pilot network formation programme (1997-1998) among indigenous industry actors. Devised through advice received from Danish experts, the programme consisted of training a team of network facilitators/brokers, and the provision of financial assistance towards the set up costs of networks between the chosen actors. After a year, seventeen networks had been established focusing on research and product/process development cooperation (Breathnach, 2001; Forfás, 2004; Edquist and Hommen, 2008).

The programme's evaluation report concluded the networks had been beneficial to the participants, and that, due to the participant firm's inexperience in collaborating with competitors, the network facilitators'/brokers' role, and patience, were vital for the programme's success. This meant that an effective framework for network promotion among indigenous firms had been established. The report proposed that a national programme for network promotion should be set up within Forbairt. However, no such programme was established. Subsequent network-related programmes introduced by

Forbairt/EI have been skills-based, e.g. Skillsnet (established in 1999) is a collaborative training programme involving collaborative networks between employers, unions and state agencies to improve workforce training particularly among SMEs (ADAPT, 2002; Breathnach, 2001; Edquist and Hommen, 2008; The Department of Enterprise, Trade and Employment, 2003).

The three research papers that jointly formed the second NESC report (1997) were commissioned to establish the suitability of applying Porter's cluster model to Irish industrial development. The authors initially struggled to find successful sectors to analyse, yet finally identified the music, dairy processing and software sectors after altering Porter's criteria for defining competitiveness. The three mini-reports ultimately found that Porter's model was inappropriate in the Irish context, as it had little validity in a small, open economy like Ireland, and that it was better suited to large mature manufacturing economies like the US and Japan, and contended that augmentations/alterations to Porter's theory would be necessary. Indeed, Porter adjusted the geographic focus of his theory in a revised edition (1998) to include non-internationally competitive regional industries, and identified significant benefits associated with closely approximated firms, e.g. competitive rivalry and the development of specialist pools of labour (Breathnach, 2001; Clancey et al. 1997; O'Connor, 1997; O'Gorman et al., 1997).

In 1998, the Department of Enterprise, Trade, and Employment (presently the Department of Enterprise, Trade and Innovation) issued a policy statement, following the formation of EI, which drew on the NESC cluster reports and the proceedings of a NESC seminar entitled 'Sustaining Competitive Advantage'. The statement concluded that the industrial base in Ireland was not suitably advanced to support industrial clusters. However, the seminar proceedings presented alternative development strategies that highlighted networks as a means to facilitate cluster development (O'Donnel, 1997; O'Brein, 2004).

In the following years, documents and statements released by EI and Forfás did not deviate from the established policy emphasis on promoting individual industry through individual firm development/cultivation, and they continued to pay lip service to the concepts of networks and clustering. This emphasis remained despite the publication of the National Competitiveness Council's Annual Competitiveness Report in 1999 which

specifically called for the promotion of networks and clusters, stating that “SMEs can be competitive if they can realise collectively the advantages of economies of specialisation that they do not have individually because of their small size” (National Competitiveness Council, 1999: 157). Additionally, the ICSTI's Technology Foresight Report (1999) recommended the development of biotechnology clusters in Ireland, though no specific development proposals were identified (Irish Council for Science Technology and Innovation, 1999).

However, over the last ten years the concepts of networks and clustering have seeped into the vocabulary of various Government Department and agencies, as evident in various publications issued since 2000. The Department of Enterprise, Trade and Employment’s 'Review of Industrial Performance and Policy' (2003) focused on developing Ireland’s economy through partnership structures focused on industrial niches. The proposed structures included features of networks and clusters. In seeking to optimise the expenditure from the NDP (2000-2006), the review called for close interactions, i.e. collaborative networks, between TNCs, indigenous companies, PREOs, VCs, regional and local authorities, and other actors. The review focused on developing niches in the software, biotechnology and digital media sectors, and highlighted the importance of SFI's CSET centres in fostering networks between PREOs and industry. Notably, the review criticised previous policies having worked against the formation of clusters in Ireland (The Department of Enterprise, Trade and Employment, 2003).

The introduction of networking into the thinking of development agencies was further advanced with the publication of two policy reports in 2004. The first report, Innovation Networks, examined the functioning of inter-firm networks internationally and in Ireland. The report stated that the government “...should focus on inter-firm networks as a key building block for the development of the innovation capacity of Irish manufacturing and internationally traded services” (Forfás, 2004: 11) and that developing inter-firm networks is “an important precursor to the formulation of policies in relation to clusters” (Forfás, 2004: 11).

The second report, 'Ahead of the Curve: Ireland's Place in the Global Economy', identified industrial networks as being key in the development of globally competitive indigenous niches. It recommended that an annual fund of €20 million be introduced to support business network developments. EI was charged with this proposal's

responsibility, yet EI's next strategy statement, covering the period 2005-2007, made only token references to networks and maintained the agency's primary focus on the development of individual firms (Enterprise Strategy Group, 2004; Enterprise Ireland, 2005; Edquist and Hommen, 2008).

Network promotion was also highlighted in the Department of Enterprise, Trade and Employment's 'Building Ireland's Knowledge Economy' (2004), an action plan for developing R&D investment. The report specifically called for the introduction of a networking- and cluster-led approach under the guidance of EI and the IDA Ireland, through focusing on specific areas "…where Ireland can develop internationally recognised applied research competencies" (Department of Enterprise, Trade and Employment, 2004: 28).

In response, EI initiated a pilot programme in 2005 to encourage research-based industry networks between companies on common topics in niche areas, including Biotechnology and NICTs. The programme demonstrated that while developing mutual research agendas among firms is challenging, the participant firms derived noticeable benefits, and that strong inter-company networks formed. In 2006, the DETE published 'Strategy for Science, Technology and Innovation 2006-2013' which mainly focused on attracting and developing FDI, yet looked towards network developments as a means of optimising NDP investment returns in PREO R&D by improving the rate of technology transfer of research through industry-led networks. It also called for the promotion of inter-firm networks, based on EI's pilot programme, yet no action was taken (Department of Trade, Enterprise and Employment, 2006).

The current National Development Plan (2007-2013) calls for the development of all-Ireland business networks and clusters to facilitate greater levels of innovation between industry and PREOs, and for the optimisation of technology transfer of PREO research. Yet, Government policy remains focused on attracting and developing FDI. The plan also calls for the development of "…niches of business in which Ireland can carve out world market leadership" (Government of Ireland, 2007: 159). To date, no real action has occurred in relation to these proposals.

In 2008, the DETE published 'Knowledge and Enterprise Clusters in Ireland', which acknowledges that networks and clusters were recommended many times since the

'Culliton Report', and comments that both concepts now form part of several on-going initiatives, including Skillnets, EI's network-related pilot programme, and InterTradeIreland's business networks. However, it also makes several statements which indicate that the concept of industrial clusters is not fully understood, including the statement that clusters have already formed in Ireland "in sectors such as ICT, bio/pharma and internationally traded services" (Department of Trade, Enterprise and Employment, 2008: 10). However groupings of firms are presented, by sectoral activities, in geographically concentrated locations as justification for such claims. No hard evidence of clustering is presented (Department of Trade, Enterprise and Employment, 2008a, 2008b).

5.4 DISCUSSION

5.4.1 Irish industrial and STI policies

The previous descriptions of Ireland's industrial and STI policies demonstrates that no co-ordination exists between both policy strands, i.e. both strands exist parallel to each other, with no co-ordination and/or complementary supports being present. This scenario has existed since the state's inception, and continues despite the development of relatively more long-term and co-ordinated funding and development initiatives since the late 1990s.

Since the adoption of open market policies in the late 1950s, the predominant focus of the state's industrial policies has been towards attracting FDI branch plants into the country, with limited policy emphasis on industrial sectoral development outside of agriculture. Successive reports from the 1960s onwards have characterised indigenous industrial firms as being small, strongly orientated around the small domestic market, and having a relatively low propensity towards innovative activities. These characteristics initially developed, in part, due to the protectionist policies which defined the country's economy until the late 1950s, and consolidated due to the minimal policy emphasis on indigenous firms, particularly relating to research-based activities, until the 1990s. Despite on-going efforts to address these issues, no culture of research or innovative activity exists among indigenous firms to cultivate (Cogan and McDevitt, 2002).

In relation to the country's science policy, limited emphasis was placed on PREO-based research activities outside of agricultural-related areas until the late 1990s. Investment levels in the country's PREOs have surged due to the various initiatives introduced

following the White Paper in 1996, yet they have had to address close to 70 years of under-investment in PREO infrastructure, equipment and skills-related areas (Cogan and McDevitt, 2002).

Additionally, the established innovative limitations of indigenous industry, allied to the branch plant nature of FDI operations, despite the introduction of more 'high-skilled' FDI activities, means that the demand for indigenous PREO-based research has been minor until very recently. This fed into, and further compounded the limited abilities of the PREOs to conduct and devise industry-orientated research activities.

Essentially, indigenous industry and PREOs have suffered decades of 'cumulative disadvantage' (NESC, 1993: 275) due to limited policy attention, the limited size of the Irish market, and their limited research and innovative capabilities. While efforts seeking to develop linkages between PREOs and indigenous industry have been introduced, no overarching policy structure exists to address the innovation paradox that presently exists, i.e. the limited abilities of PREOs to engage in, or diffuse commercially-orientated research activities, and the limited absorptive capacity, or ability of indigenous firms to engage in such activities.

Additionally, the Government's industrial policies remain focused on FDI-related firms/sectors, particularly in seeking to attract more complex R&D-related FDI operation into the country. While more advanced FDI activities have been introduced, their linkages with the indigenous economy remain limited. Recent developments, e.g. the relocation of Dell's Limerick-based activities to Poland, have again exposed the vulnerability of this policy focus and approach.

Barry (2006) commented that if “Ireland's ability to attract FDI were to deteriorate for any reason…(e.g., through a shift in US corporate strategy or a change in US tax laws), the country could be thrown back onto the resources of indigenous industry...[which] remain quite weak” (Barry, 2006: 54). In 2009, the US Government announced plans to remove 'deferral rules' that allow American firms defer reporting income generated in their non-US operations to the US Internal Revenue Service, and to claim tax credits for paying foreign taxes, i.e. tax exemptions or deductions on their US tax bill on, for example, investments on their non-US based factories. This development could have substantial impacts on existing FDI operations in Ireland, particularly if the changes to

the US tax system are extended (Staunton and Hancock, 2009; Fey, 2009).

Additionally, recent decisions by different TNCs to restructure their global operations, in part due to the rising cost base of operating in Ireland, have had substantial impacts on the economy, e.g. Pfizer's announcement that it would close three Irish-based manufacturing plants in 2010 (The Irish Times, 2010).

5.4.2 Network- and Cluster-related policies

Until recently, the concepts of networks and clusters did not feature in Irish industrial policy despite many reports since the early 1980s calling for their introduction. These concepts have entered the vernacular of Government agencies over the last 10 years. Yet, despite their increased prominence, no programme seeking the development of networks and/or clusters has been introduced due to an absence of commitment from the Government.

There seems to be limited understanding of what both concepts are, judging by recent reports released by the Department of Enterprise, Trade and Employment. Networks are presented as a mix between business networks, i.e. quasi-social 'networking', and inter-actor networks. In relation to clusters, no real evidence exists that the concept is fully understood, e.g. geographic proximity among some industry firms, with no regard for the nature of their interaction, is seen as being sufficient to declare such groupings as clusters.

A major issue potentially hampering cluster-related policy formulation is that the regional aspect of clusters runs counter to the long established centralist structure of the Irish Government. From the state's inception until 2002, no clearly defined regional aspect to Irish Government structures, policies or programmes existed, while the government and its administration remains highly centralised around the GDA.

One of the first calls to introduce regional aspects to Government policies was through the publication of a Government report, 'Regional Studies in Ireland' (1968), commonly referred to as the 'Buchanan report' after its author Colin Buchanan. This report sought to formulate economic development proposals with an explicit regional focus. It stated that Ireland's future economic development would concentrate around the GDA, and proposed that industrial development should concentrate in a limited number of development centres throughout the country in an effort to counterbalance the GDA's

magnetism. Less then a dozen locations were identified as being suitable for these centres, meaning the report's proposals received little public, and crucially, political support. Its findings were essentially shelved, and subsequent FDI activities were geographical dispersed, predominately in response to political concerns (Bradley, 2000; Dempsey, 2001).

It wasn't until 2002 that a defined regional focus was introduced to Government policies with the publication of the National Spatial Strategy (NSS) (2002). The NSS was a long-term (20 year) strategic vision for Ireland's future spatial development. It detailed an overreaching national framework for balanced regional development for the various policies, programmes and investments of the relevant government departments and agencies. However, it was unclear as to how elements of the strategy should be implemented (NSS, 2002).

The NSS was formulated in response to the majority of the 'Celtic Tiger' related developments being focused and located in the GDA, as predicted by the Buchanan report. Due to Dublin's position as Ireland's capital city and centre of political activity, it has always been the country's key economic centre. As stated above, Dublin's importance to the Irish economy deepened during the 'Celtic Tiger' era, resulting in a significant imbalance between the GDA and the rest of the country (Brennan, 2007; Clark, 2008; Goodbody Economic Consultants, 2007).

The NSS called for balanced regional development in a polycentric urban structure, i.e. that all regions should contribute to the optimal economic, social and environmental performance of the state as a whole. The strategy was structured and organised around the concepts of gateways, i.e. designated key urban centres whose critical masses of economic activity would drive the development of urban areas and their surrounding regions, and hubs, i.e. strategic regional centres that would invigorate their immediate surroundings and act as links between the gateways and rural areas. The gateway cities would act as the economic drivers of their regions, acting as a counter-balance to the GDA, and at the same time complementing it (Cooke, 2002: Department of Trade, Enterprise and Employment, 2003; NSS, 2002).

The NSS emphasised the importance of regions in Ireland's future economic development. Despite the increased influence and importance of globalisation to

economic development, regions increasingly play central roles in determining a country's economic performance, i.e. high-value, high-innovation enterprises optimally develop in areas where there exist concentrations of enterprises, skills, infrastructure, and services, and PREOs with well-developed capabilities in their particular field. By developing gateways and hubs, the NSS aimed to increase the locations in Ireland that could offer a viable and attractive location for advanced high-technology enterprises (Cooke, 2002: Department of Trade, Enterprise and Employment, 2003).

While the NSS contained no concrete proposals for developing industrial clusters, it did provide a rationale for concentrated spatial development upon which such policies could be developed, i.e. regional structured innovation/enterprise supports to facilitate the development of regional specific cores of knowledge and human capital, and varieties of networks that facilitate innovation and ultimately lead to cluster formation. Essentially, through developing and exploiting existing regional differentiations within a dedicated regional support framework, the NSS, as a very bare framework, presented a potentially useful model for an over reaching, network and cluster orientated development policy programme in an Irish context.

However, funding for the Gateways Innovation Fund Programme, the NSS's centre component, was deferred in 2008 as the Government sought to cut public spending following the post-Celtic Tiger economic slump. No indication of the funding being re-established, or of the formulation of a replacement programme, has been made to date (Tansey, 2008).

5.4.3 Biotechnology specific policies

Following the emergence of the modern bio-sector in the mid 1970s, governments in many developed economies identified biotechnology as playing an important role in their future economic development.

The Irish Government first identified biotechnology's importance for Ireland's future development in the late 1970s, yet serious and sustained efforts to develop a significant indigenous bio-sector were not introduced until the late 1990s. These initiatives have focused on facilitating developments in the country's PREOs. To date, no defined or co-ordinated policy programme has been developed that targets the entire bio-sector's development as a whole, i.e. biotechnology-related initiatives remain dispersed among different industrial and STI policies, no joining up of interrelated policy strands has

occurred.

The bio-sector’s value chain is inherently network structured, while the international bio-sector's key hubs are industrial clusters. The absence of a defined network approach towards sectoral development, despite various Government reports identifying them as crucial features in the development of the international bio-sector, and the absence of defined regional aspect to current development initiatives are significant issues.

Essentially, the uncoordinated industrial and STI policy strands, combined with the absence of network or cluster elements to these policies, demonstrates that the Irish Government's current policy approach towards developing the indigenous bio-sector is not suitably, or optimally focused towards the bio-sector's needs.

Using the key points made in this discussion, the focus of the thesis now turns towards an analysis of the indigenous sector's network structure.

CHAPTER 6:
ACTOR TYPOLOGIES IN IRELAND'S INDIGENOUS BIOTECHNOLOGY SECTOR

6.1 INTRODUCTION

This chapter applies the international biotechnology sector's (bio-sector) actor typologies to the Irish bio-sector, so as to identify the features, characteristics, and development trends of indigenous actors in relation to those found in the international bio-sector. The chapter is divided into two sections. Section one details the evolving nature and characteristics of the indigenous bio-sector's actors, in relation to the impacts of previous and on-going public sectoral development initiatives. Section two discusses the structure of the Irish bio-sector and how it compares to the actor typologies and sectoral structures in the key international bio-sectors, as detailed in chapter 3, in the contexts of the evolving characteristics of the actors themselves and the role of government initiatives in their development trajectories. The methodology employed in compiling these typologies was detailed in Chapter 4.

6.2 ACTOR TYPES IN THE IRISH BIO-SECTOR

The following actor typologies were derived from an augmented and up-dated version of typologies developed by Barley et al. (1992) and from observable patterns in the international bio-sector (as detailed in Table 6.1). It must be noted that all of the sectoral actor types are important in the sectoral value chain, acting as either incubators or transfer mechanisms within the bio-sector's innovation process. They are detailed separately below solely for ease of presentation.

6.2.1 Public Research and Education Organisations

Very limited Government investments occurred in the infrastructures, facilities, resources or skill sets of Ireland's PREOs over an almost 70 year period, prior to the mid 1990s. This was due to the different Science, Technology and Innovation (STI) policies over this period predominantly focusing on supporting the country's agricultural and food sectors (as detailed in the previous chapter) (Acheson, and Lambkin, 2009; Burke et al, 2003).

Irish Government STI policies began in earnest from the 1960s onwards, yet very limited research grants and/or infrastructural investments were introduced. Indeed, the majority of STI policy-related developments from the late 1970s onwards were supported and/or motivated by a variety of European Economic Community/European

Union programmes, particularly the different Framework Programmes. As such, entrenched institutional inertia co-existed with structural inflexibilities, i.e. the individual PREO actors types were clearly differentiated, and had relatively little resources to develop research facilities and/or programmes (Acheson, and Lambkin, 2009; Cordis, 2006; Forfás, 2004).

In the wake of the publication of the 1996 White Paper on Science, Technology and Innovation, the Irish Government identified biotechnology as being crucial for Ireland's future economic development. Since the late 1990s, sustained public investment programmes, particularly the Programme for Research in Third Level Institution (PRTLI) and the Technology Foresight Fund (TFF), have targeted the formation of an advanced PREO-based science base as a central element in the development of the indigenous bio-sector, and have facilitated substantial research infrastructure, resource, and skills-related developments.

There are presently eight Universities (including the Royal College of Surgeons in Ireland), 14 Institutes of Technology (IoTs), 37 PREO-based research institutes (RIs) and 12 research hospitals (RHs). The largest concentration is in the Greater Dublin Area (the GDA), followed by Counties Cork and Galway (Figure 6.1).

6.2.1.1 Universities

The level of university-based research in the Irish bio-sector was restricted by the limited infrastructures, resources and skill sets which had developed due to the limited investments in the PREOs until the introduction of the on-going development programmes in the late 1990s. As detailed further in the following chapter, these issues undermined the commercial developments in the indigenous bio-sector.

Since the late 1990s, the capabilities of Universities have advanced due to the on-going public investment programmes. However, it must be noted that such developments have been limited relative to those of the RIs, due to the pronounced RI focus of these programmes (detailed further in the following section).

There are eight Irish universities (Figure 6.1), employing close to 500 academic staff in biotechnology-related subjects. Annually, around 500 students graduate from the universities' biotechnology/biotechnology-related undergraduate and postgraduate

Table 6.1: The bio-sector actor typologies

Public Research and Education Organisations (PREOs): Commercial biotechnology developments in the international bio-sector are predominantly based upon findings from the research programmes of PREOs, they also facilitate complex tacit and codified information exchanges, and crucial sectoral skills developments and transfers. There are three PREO actors:

- Universities are the main source of the basic research from which commercial biotechnology activities are derived. Academic departments primarily focus on long-term speculative/exploratory basic research, which is important for volatile technology sectors, by being less subject to market pressures then commercial actors. Universities actively promote information transmission by adhering to "the [traditional] norms of the open information disclosure characteristic of public science" (Smith and Powell, 2004: 8) through lecturing, publications, and placements. They also provide undergraduate and research-orientated postgraduate education programmes.
- Public Research Institutes (RIs): Typically established by university academics in association with government departments/agencies to develop themed research programmes based on their areas of expertise, RIs typically locate in close proximity to their 'parent' university/universities. The focus mainly on applied research; many commercial developments originate from RIs as governments seek, internationally, to engender such developments though facilitating formal alliances with commercial actors via defined commercialisation supports and infrastructures.
- Research Hospitals (RH): RHs focus on specialised medical research, engaging in application-based diagnostic and therapeutic activities. RHs associated with a 'parent' university are typically located in close proximity. RHs are significant actors in the sector's innovation process by being the main source of clinical research trial samples, and are also involved in the clinical trials of new biotechnology-based therapeutics and diagnostics products, through joint research programmes with bio-firms and/or TNCs or via in-house laboratory research. RHs are among the main customers of biotechnology-derived pharmaceutical products and services.

PREOs increasingly seek commercial developments from their activities, and have developed advanced commercialisation procedures to optimise research transfers to commercial concerns. These mechanisms include pronounced commercial elements in education programmes to inculcate/encourage commercial mind frames among researchers, industrial liaison offices (ILOs) seeking to identify viable research into link into firm-based research programmes, technology transfer offices (TTOs) proactively seeking to transfer IP to commercial actors (some US and UK TTOs are independent entities whose survival depends on successfully commercialisation), and the development of bio-incubators (located in close proximity to RIs) to optimise firm developments through training, development, financial support services.

Biotechnology firms (Bio-firms): The bio-sector's innovation process, and key informal and formal networks, can be separated into two broad categories, upstream and downstream activities, relative to a firm's position in the sector's value chain. PREO research can be conceived as the upstream end of the value chain. Firms seek to engender informal and formal relationships with PREOs to access and commercialise research. The clinical trials process and sale to the consumer can be conceived as the downstream end, i.e. predominately formal network-based interactions with TNCs and other firms. Bio-firms traditionally occupy the middle rung in the sector's innovation process, being the main transferring mechanism of PREO research to the market. They draw on heterogeneous communities of experts at various points in their development, and are established by PREO researcher to pursue research exhibiting clear commercial promise to develop commercial products and services in a wide variety of research areas (yet, overwhelming in pharmaceutical-orientated research). Their development is determined through formal alliances with investor actors, particularly Venture Capital firms, to finance their start-up and initial developments prior to forming alliances with downstream actors. A firm's ability to access PREO-based knowledge and VC funding are the determinants of its research capabilities and its success in commercialising research through commercial actor alliances.

Investors: The technical and financial resources required to develop biotechnology products are beyond the capabilities of most bio-firms as, in comparison to other high-tech intensive sectors, development costs in biotechnology are significantly higher, e.g. product development can take up to 20 years and cost up to US$1 billion. Different investor types play particular roles in the product development process:

- Personal and Private funding sources: Due to their high risk nature, bio-firms often cannot access traditional finance sources, e.g. bank loans, meaning their set-up stages are often financed through personal and private funding, i.e. personal savings, private loans from friends/family, and non-business bank loans offset by the value of their intellectual property.
- Public and Private Venture Capital firms: VCs have played central roles in the international bio-sector's development since its inception. Typically established by wealthy private investors or by governments seeking to develop indigenous sectors, they target relatively unproven businesses traditional investors (e.g. banks) avoid due to high-risks or excessive development costs. VCs are compensated through equity securities in a firm in return for an investment, and thus a portion of capital gains when the firm is traded on stock markets through an Initial Public Offering (IPO) or bought up/bought into by a TNC (the main exit strategies for VCs in bio-sectors). VCs provide managerial and technical expertise to optimise a bio-firm's business development (academic researchers normally receive minimal education/training in business-orientated subjects), and new management structures can be sought to deal with the complexities of negotiating downstream alliances/collaborations. Several issues with VC funds motivates bio-firms *and* VCs to seek exit strategies, including a mismatch between the typical length of a VC alliance (5 years) and the biotechnology product/process development cycle's duration (approximately 15 years), while VC funding oscillates due to the relative performance of global economies and other industries.

Diversified Transnational Corporations (TNCs): TNC involvement in the international bio-sector predominantly focuses on pharmaceutical activities as the 'tradition' knowledge base they derived products from (organic chemistry) is reaching its technological development limits. Biotechnology draws from a different knowledge base (immunology and molecular biology) whose limits have yet to be clearly defined, and is easily adaptable to TNC requirements, meaning it is increasingly the basis of new pharmaceutical products/treatments. As the development costs and duration of new drugs is increasing due to stringent regulatory requirements, which impinge on TNCs recouping their development investments, and as effective patent-protection on traditional products is being impacted by generic products, TNCs are focusing on small volume niche market drugs, new versions of existing drugs, and have moved from mono-product to 'flexible' multi-product production. TNCs collaborate with bio-firms to optimise product development activities and fill their product development pipeline, which represent the main downstream relationships of the sector's innovation process.

Government Departments and Agencies: Many industrialised nations have identified biotechnology as key to their future economic development. Governments are increasingly crucial in providing funding to drive sectoral developments. Such funding can be typified as being primarily PREO focused, through resource and capital investment programmes/initiatives in the research capabilities and infrastructures of PREOs. Governments are also placing increased commercial emphasis on PREO activities to drive sectoral developments, and have created dedicated public VCs funds to address speculative funding shortages in sectors.

Additional actor types:

- Supply firms facilitate research and production activities, service suppliers provide specialised systems and solutions to different issues arising in research.
- Sub-national Biotechnology Centres are typically created by business associations to optimise a region's network structure and density, and disseminate important region-specific information among sectoral actors.
- Trade associations focus on specific sectors/sub-sectors, not particular locations, circulating sector-specific information and providing services to their members'. They can construct brands to improve a sector's profile, and act as lobbyists.
- Private Research Institutes are usually founded by wealthy benefactors to fund research in areas that receive little commercial attention, but are judged to have social value.
- Repositories (Gene Banks) are stores of genetic resources that seek to maintain genetic diversity by capturing a genetic picture at a particular point in time, and are important for future research projects, particularly genomic research.

After (Burke et al, 2003; Owen-Smith and Powell, 2007; Prevezer and Tang, 2008; Gertler and Levitte, 2005; Powell and Brantley, 1992; Barley et al., 1992; Stuart et al., 2007; Giesecke, 2000; Feldman and Braunerhjelm, 2007; Ernst & Young, 2007a; Ahrweiler et al., 2011; Lee, 2012; Eisingerich et al, 2012).

courses. These courses cover a diverse range of biotechnology/biotechnology-related subjects including genetics, biology, biochemistry, micro-biology and molecular biology (see Appendix D for full details) (Forfás, 2001; Morrissey, 2011).

Within the universities, Forfás (2003) noted specific areas of excellence in the following biotechnology-related areas:

- biochemistry and molecular biology,
- microbiology and chemistry, and
- veterinary sciences, neurosciences, biotechnology and applied microbiology, and genetics (Forfás, 2003).

6.2.1.2 Institutes of Technology

The country's IoTs were initially established as Regional Technical Colleges (RTCs) in 1968, following the creation of the National Research Council in 1967, so as to "meet the technical training needs of [the] newly arrived multi-national manufacturing industries" (Acheson, and Lambkin, 2009: 3) attracted into Ireland through the adoption of open market policies in the late 1950s. Historically, the RTCs focused more on providing training courses in specific activities, e.g. laboratory technician training, rather than on research.

In 1999, the RTCs were renamed IoTs, and their focus changed as government agencies sought to exploit their untapped scientific resources. Through PRTLI funding, their research activities have expanded, yet to a limited degree. To date, only two IT-based RIs have been developed in biotechnology-related areas (detailed in Appendix D) due to the development initiatives overwhelming focusing on the development of university-based RIs (Higher Education Authority, 2004, 2007).

6.2.1.3 Public Research Institutes

A small number of (relatively) adequately funded and supported PREO-based RIs were formed during the 1980s, i.e. the five BioResearch Ireland RIs created in 1987 through the National Biotechnology Programme (NBP) (detailed in the previous chapter), and several Teagasc's RIs (discussed further below). The BioResearch Ireland RI's were initially intended to develop downstream links with the indigenous bio-sector by engendering the emergence of start-up bio-firms, yet they were ultimately established as independent entities from the departmental structures of their 'parent' universities, and subsequently failed to develop/feed into significant downstream developments, in part

due to the presence of a significant innovation paradox among the RIs and the wider bio-sector (Forfás, 2004).

Following the introduction of the PRTLI and the TFF, 26 RIs have been established (Figure 6.2). Government agencies view these RIs as being key elements in the indigenous bio-sector's development, mirroring the characteristics of RIs in the international bio-sector. The RIs have been specifically created with inter-institutional structures, and proactively target the development of extensive networks/collaborations with downstream actors, as their long-term survival is dependent on generating money from successful commercial ventures, i.e. they are only fully funded for five years, with no default budget, after which they are expected to become self-sufficient entities by generating revenue streams via commercial alliances (Higher Education Authority, 2006, 2007; Morrissey, 2011).

6.2.1.4 Research Hospitals

Until the late 1990s, hospital-based research was essentially an untapped resource in the indigenous bio-sector as these institutions received limited funding, and they conducted minimal research activities as a result. In the context of the indigenous bio-sector's limited commercial activities (detailed further below), Irish hospitals essentially had no involvement in commercial activities.

Since the late 1990s, hospital-based research activities have increased with the development of several RHs and bio-incubators. There are currently 12 biotechnology-related research and teaching hospitals (Figure 6.2) affiliated to Irish PREOs, eight in the GDA, and two each in Cork and Galway (discussed further in Appendix D). A key RH development was the establishment of the Dublin Molecular Medicine Centre (DMMC) in 2002, through PRTLI and the National Development Plan (NDP) (2000-2006) funding, which links three Dublin-based universities and six RHs (Higher Education Authority, 2006; Dublin Molecular Medicine Centre, 2007a).

6.2.1.5 The commercial orientation of Irish PREOs

The commercial orientation of Irish PREOs, prior to the late 1990s, was poor due to a combination of factors, i.e. the limited nature of the commercialisation support procedures and infrastructures of all the PREOs, the limited commercial orientation of administrators and academics, and the limited emphasis on the commercialisation of PREO activities by Government actors. This scenario fed into, and was compounded by

the limited levels of downstream sectoral activity.

Following the introduction of the on-going Government initiatives, significant improvements have occurred in the commercial orientation of the country's PREOs. These developments include the development of more advanced and proactive commercialisation procedures and infrastructures in their TTOs and ILO, while five innovation centres, i.e. incubators, have also been introduced:

- the INVENT incubator located at DCU (opened in 2004);
- the NovaUCD incubator located at UCD (opened in 2005);
- the Trinity Bioincubator located at TCD's Enterprise Centre (opened in 2004);
- the NUIG Bioincubator (opened in 2004), and;
- the Bio-incubation Centre located at UCC (opened in 2004) (Forfás, 2008; Enterprise Ireland, 2005a, 2005b, 2005c, 2005d, 2005e).

These incubators replicate features of their counterparts in the international bio-sector, i.e. they provide laboratory space and financial and business supports in legal, marketing and management areas so as to facilitate the emergence of innovative commercial entities originating from PREO research. The incubators were established through funding and support from Enterprise Ireland (EI) and Enterprise Ireland's Biotechnology Directorate (EIBD), and have had substantial impacts on the commercialisation of PREO-based research, particularly through the recent RI developments (Forfás, 2008; Enterprise Ireland, 2005).

Additionally, Science Foundation Ireland (SFI) established Centres for Science, Engineering & Technology (CSETs) in 2003. The CSETs assist the development of alliances between scientific and engineering PREO-based researchers and industrial actors, so as to develop new and existing Irish technology-based companies. Of the eight CSETS, four are engaged in biotechnology/biotechnology-related activities (Alimentary Pharmabiotic Centre, 2007: Forfás, 2004: The Irish Scientist, 2003: University College Cork, 2003: Science foundation Ireland, 2002, 2007).

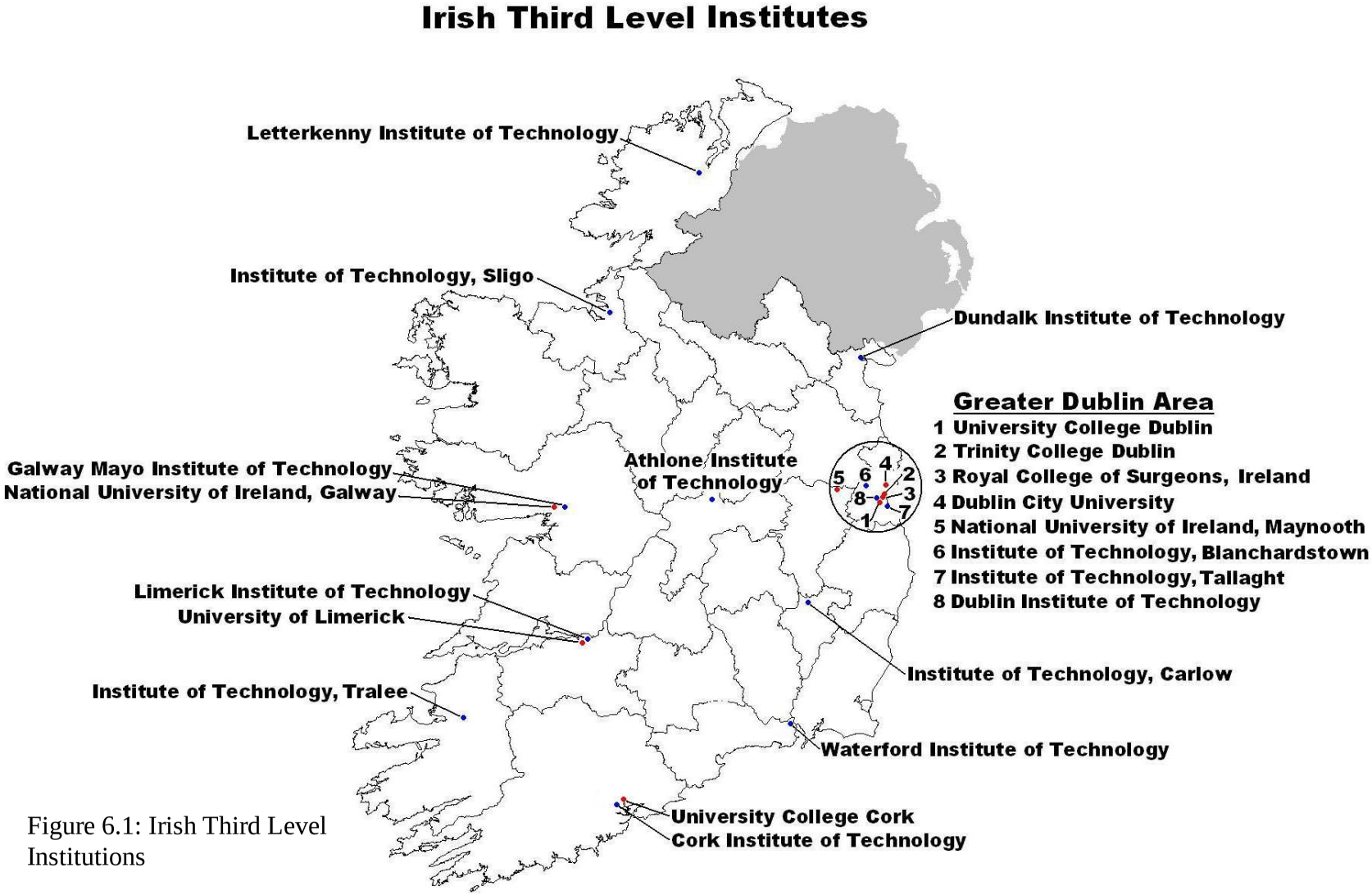


Figure 6.1: Irish Third Level Institutions

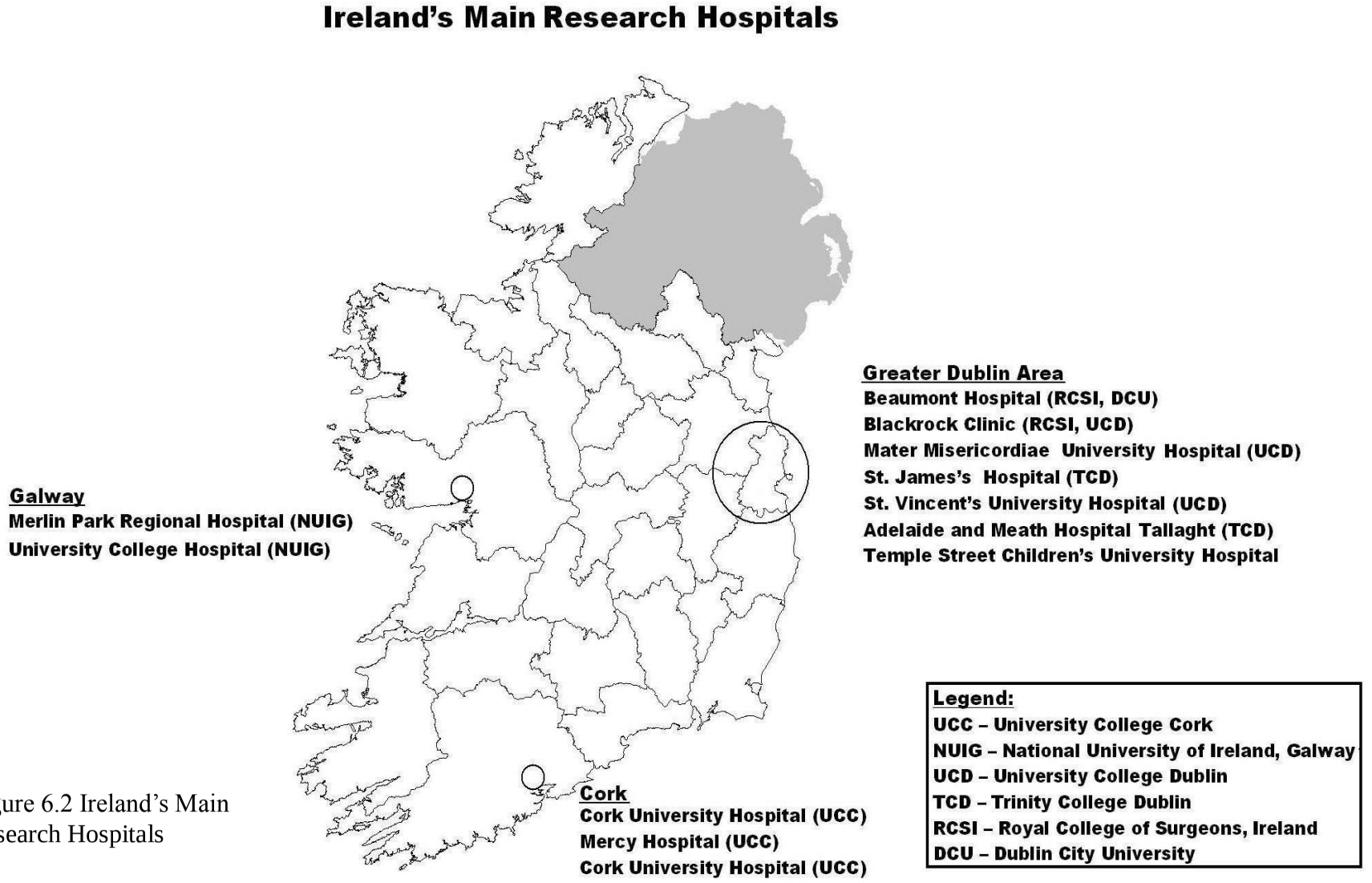


Figure 6.2 Ireland's Main Research Hospitals

The improved commercial supports and orientation of the PREOs has resulted in a relative surge in commercial activities, in particular a dramatic increase in the number of start-up bio-firms originating from RI-based research over the last 10 years. This is detailed further in the following section.

6.2.2 Biotechnology firms

A very small number of indigenous bio-firms were established prior to the development of the modern bio-sector in 1976 in areas that subsequently became biotechnology-related sectors, e.g. pharmaceuticals and food processing. Following the development of commercial biotechnology technological applications, these firms began to adopt biotechnology processes/technologies and to develop biotechnology activities. Subsequently they abandoned their 'traditional' technological platform(s) completely in favour of biotechnological applications and procedures.

In relation to 'traditional' bio-firms, there exist two distinct tiers in the indigenous bio-sector, i.e. those formed before and after the introduction of the various sectoral development initiatives in the late 1990s which followed the publication of the White Paper on Science, Technology and Innovation in 1996 (in particular the Programme for Research in Third Level Institutions and the Technology Foresight Fund, as detailed in chapter 5). From here on, depending on when they were established, the indigenous firms are referred to as pre- and post-initiative bio-firms. Indeed, it must be noted that the pre- and post-initiative divides presented in this chapter, and in the remaining chapters, also refer to these time periods.

In 2000, there were thirty Irish firms in the bio-sector. As with firms in the international bio-sector, they were predominantly established by commercially-minded PREO-based researchers that identified either a domestic market opportunity, e.g. the relative absence of diagnostic services, or a specific technology that had obvious commercial potential. However, as these pre-initiative bio-firms developed when the indigenous bio-sector was characterised by substantial structural weaknesses, they were very high-risk ventures for several reasons (Morrissey, 2011).

In particular, the bio-firms emerged in the context of poor levels of entrepreneurial/commercialisation experience and supports among the PREOs (as detailed above), which resulted in many bio-firms buying their Intellectual Property (IP) from non-Irish PREOs. Additionally, due to the virtual absence of 'traditional' bio-sector

funding sources, i.e. a small and sceptical local VC community (detailed further below), these bio-firms relied mainly on private donations and substantial personal loans. In the very limited number of cases where bio-firms accessed speculative investor funding, they were with non-local investors, particularly US- and UK-based actors (BioResearch Ireland, 2001b).

These issues resulted in the pre-initiative bio-firms adopting very conservative business models. Many bio-firms deliberately targeted slow growth rates and very narrowly defined niche areas, i.e. diagnostic-related activities, to side-step these issues, and offered services to commercial actors so as to finance their core R&D activities and maintain turnover. Overall, the operations of the majority of pre-initiative bio-firms were (and remain) limited in size and scope, while their narrowly defined activities meant they were not research focused/orientated. These issues resulted in a very limited number of pre-initiative bio-firms successfully developing products/processes in diagnostics and pharmaceutical biologicals areas (Malecki, 1997; Morrissey, 2011).

In contrast, the post-initiative bio-firms can be characterised as 'Genentech template' start-up bio-firms, i.e. they emerged in the context of significant RI-based activities, and in the presence of advanced PREO-based commercialisation supports and dedicated biotechnology VC funds (discussed further below). However, due to their age and relative state of development, they are small in size and have yet to engender significant commercial activity. Additionally, they are engaged in therapeutic and platform technology-related activities, which means no firm-based drug development activities have occurred to date in the Irish bio-sector.

There are presently 66 indigenous bio-firms engaged in biotechnology/biotechnology-related activities. The largest concentrations of bio-firms are in the GDA (28 bio-firms), the Cork City region (13 bio-firms), and the Galway City region (7 bio-firms). The bio-sector employs over 500 people directly, and the indigenous bio-firms generated over €430 million in turnover in 2003, yet the majority of this was accounted for by a very limited number of bio-firms (InterTradeIreland, 2003; Enterprise Ireland, 2005; IDA Ireland, 2007; Morrissey, 2011).

Table 6.2 shows the sub-sectoral breakdown of their activities, and the number of bio-firms involved in each activity in 2009. Irish bio-firm activities are overwhelmingly

pharmaceutically-orientated, yet the bio-sector's activities are quite varied, covering most areas of current biotechnology activity. There are a limited number of specialist supply firms in the bio-sector, e.g. platform technology and specialist research bio-firms. This may appear to reflect trends of vertical integration found among bio-firms internationally, yet the nature of their linkages with other sectoral actors is restricted due to the bio-sector's limited size and activities. Their activities are very narrowly focused due to conservative business models, and in one case a supply bio-firm is essentially an 'independent' subsidiary of a PREO (BioResearch Ireland, 2001; InterTradeIreland, 2003).

Table 6.2: Activity focus of the Irish bio-sector's bio-firms

Bio-firm Type	Bio-firm numbers	Descriptions of bio-firm activities
Pharmaceutical-biologics bio-firms	23	Bio-firms which develop biotechnology-based vaccines and types of therapeutics.
Pharmaceutical services bio-firms	11	Bio-firms which provide services to the pharmaceutical-healthcare sector, including the provision of recombinant proteins and recombinant production services.
Diagnostic bio-firms	17	Bio-firms which make measurement devices for diagnosing particular diseases or their resulting consequences.
Agri-food bio-firms	9	Bio-firms that are engaged in the development of applications, including the production of biological materials, specialist products for human food or animal feed, and specialist cultures.
Bio-environmental bio-firms	6	Bio-firms which provide services focusing on the detection, prevention and/or clean-up of environmental damage. Their major products are based on microbial cultures.

Based on InterTradeIreland (2003).

The bio-sector's age structure reflects the limited/restricted nature of the pre-initiative bio-firms and the relative age and state of development of the post-initiative bio-firms. The majority of the bio-firms are less than twenty years old, which means very few have reached the product/process development stage. Indeed, almost all of the survey respondent bio-firms stated that around 80% of their workforces were engaged in research. The overall level of commercialisation activities in the Irish bio-sector, to date, has been minor (Burke et al, 2003; Ernst & Young, 2003; InterTradeIreland, 2003).

6.2.3 Investors

Until the introduction of the various development initiatives in the late 1990s, investor involvement in the indigenous bio-sector was limited due to its small size and restricted commercial activities, and the associated restrictions on development opportunity these issues caused. As such, investors were very sceptical of the bio-sector's commercial promise. Pre-initiative bio-firms relied heavily on private funding sources, as Irish VCs mainly focused on sectors with more obvious commercial potential, in particular ICT sector-related opportunities. It must be noted that no dedicated VC firm existed to

service the indigenous bio-sector until 2001 (Forfás, 2004).

In alliance with the various on-going PREO-based funding programmes, several dedicated biotechnology VCs have been developed by public actors to address the relative absence of investor actors in the bio-sector and to drive commercial sectoral developments. These VCs have facilitated the surge of 'Genentech Template' post-initiative bio-firms, as detailed above.

The first dedicated VC, Seroba BioVentures, was established in 2001 under EI's biotechnology strategy as an investment development firm. Its investment fund totalled €20 million, and sought to facilitate start-up bio-firm development from PREO-based research in the areas of therapeutics, medical devices and diagnostics, and new enabling technology platforms. Seroba was re-launched as Seroba Kernel in 2009, under EI's Seed and Venture Capital Scheme 2007-2012 (discussed below) (Seroba BioVentures, 2005; European Venture Capital Journal, 2009).

Also in 2001, private investment company Growcorp was established by the Department of Enterprise, Trade and Employment (with funding provided through EI's Seed and Venture Capital Programme 2001-2006, discussed below), accountancy service firm PriceWaterhouseCoopers and private donations from the Irelandia Investment group to exclusively target the life science sector through its European Bioscience fund, which amounts to €25 million. Growcorp differs from Seroba Kernel by providing wet-lab space and specialist business services, including marketing and financial planning services/advice to its target bio-firms (Smyth, 2003; Enterprise Ireland, 2004).

The number of VCs investing in the indigenous sector has subsequently increased due to successive EI co-ordinated Seed and Venture Capital Programmes in 2000-2006 and 2007-2012. The 2000-2006 programme, created under the NDP 2000-2006, provided €98 million to 15 VC funds established under the previous EI VC programme (The EU Seed and Venture Capital Measure 1994-1999) to "...develop the venture capital market for [Small to Medium Enterprises] in Ireland" (Enterprise Ireland, 2005; 3). The follow-on programme (2007-2012) is funded to a level of over €170 million, under the new NDP 2007-2013 (Finfacts Ireland, 2007; The Department of Enterprise, Trade, and Employment, 2006; Morrissey, 2011).

Among the biotechnology/biotechnology-related VC funds supported by EI are:

- Enterprise Equity Venture Capital: established in 1987, it launched a €7million seed capital fund in 2003 for early stage technology companies,
- Delta Partners: established in 1994 with a fund of over €60 million, it focuses on early stage companies in high-tech sectors including the bio-sector,
- HotOrigin Fund I: established in 2001 with a fund totalling €2.3 million targeted towards Bioinformatics and new information and communication technologies (NICT) firms,
- 4th Level Ventures: established in 2004 with a fund of over €17 million, and
- AIB Seed Capital Finance: established in 2007, and located on the UCD campus. The firm's fund totals €30 million, half from EI, the remainder from AIB (Enterprise Ireland 2006, 2007).

The net effect of the EI-sponsored programmes has been a substantial increase in VC involvement in the indigenous bio-sector, and the resultant development of the 'Genentech Template' post-initiative bio-firms. However, the relative level of VC investments in the bio-sector, in comparison to other similarly sized and emerging bio-sectors, "...has been on a very minor scale so far, and much of it has been focused on service companies in supporting roles such as clinical research services and clinical data management, rather than on [drug discovery] biotechnology start-ups" (Technology Ireland, 2004: 10).

Additionally, the Irish VCs are overwhelmingly concentrated in the GDA. Despite their nationwide scope, over half of the VC investments in the indigenous bio-sector were made in the GDA by 2006. This has created discrepancies in how the bio-sector has developed regionally (Enterprise Ireland, 2005; Dodgson et al., 2008; Chen at al., 2011).

6.2.4 Diversified Transnational Corporations

TNCs first established operations in Ireland following the Government's decision to create an Irish industrial export base by attracting Foreign Direct Investments (FDI) after abandoning protectionist policies in the late 1950s. Since the early 1970s, the Irish-based operations of pharmaceutical TNCs have been of great importance to the Irish Economy.

Yet, TNC operations in Ireland until the mid 1990s were predominantly commercial-

scale manufacturing-orientated branch plants that exported the vast majority of their output, and which developed very limited alliances with the indigenous economy. Their product and production processes would be fully developed in their home countries, after which process would be transferred to the commercial scale facilities in Ireland (van Egeraat, 2009; Girvin, 1983; Honohan and Walsh, 2002).

Since the mid-1990s, Irish-based TNC operations have changed in form, in part due to proactive efforts by the relevant Government agencies to attract more high-tech skills intensive TNC activities into Ireland (discussed further below). These developments also reflect international trends in TNC operations:

- TNCs have re-organised their production activities by focusing on smaller volume niche market drugs,
- TNCs have also sought to improve the efficiency of their process R&D activities by moving away from mono-product production processes towards 'flexible' multi-product production processes which involve more process R&D activities,
- TNCs have responded to the combined impacts of increasingly stringent regulatory requirements expanding the time and costs of new drug developments and the declining effective period of product patents, due to the emergence of generic pharmaceutical products, by adopting more biotechnology-based practices in their production plant activities to advance their product development processes (van Egeraat, 2009; Ernst & Young, 2007).

As such, additional functions have been added to Irish TNC operations, notably process R&D activities in biopharmaceutical-related activities.

The TNC sector in Ireland presently includes manufacturing operations of 13 of the world's top 15 pharmaceutical firms, including Roche, GlaxoSmithKline and Wyeth. According to IDA Ireland, 120 overseas pharmaceutical and chemical companies were located in Ireland, employing over 20,000 people with combined exports totalling over $35 billion annually in 2006. This accounted for over 30% of total national exports, second in value to exports from the engineering/electronics sector (BioResearch Ireland, 2000: Forfás, 2003: IDA Ireland, 2005, 2006; Morrissey, 2011).

Recent R&D orientated developments in the operations of TNCs have resulted in Ireland emerging as a key location for biopharmaceutical active ingredient plants over

the last eight years. These developments include:

- Pfizer established a €2 billion biopharmaceutical campus in Newbridge, County Kildare in 2003, creating the largest biotechnology plant in the world. The facility engages in drug development, process development and large scale production. Wyeth collaborates with a number of RIs, including the Irish Centre for Applied Neurotherapeutics, and the National Institute for Cellular Biotechnology,
- Schering-Plough has established research facilities in Cork and Wicklow. The Cork biotechnology plant engages in R&D on process development activities, including phase II and III clinical trials of new products. The Wicklow R&D operation is involved in process development and analytical methods in the development of drugs in Phase II & III clinical trials, and also manufactures clinical trial quantities of new drugs in a pilot production plant,
- Eli Lilly's biopharmaceuticals manufacturing facility in County Cork,
- Bristol-Myers Squibb invested €9.6 million in 2005 to establish collaborative biopharmaceutical research facilities located at Dublin City University and the National University of Ireland, Galway,
- Genzyme invested over €6 million in 2001 to expand process R&D activity in its Waterford plant, and
- Boston Scientific established a Galway-based R&D operation in the mid 1990s which is engaged in the product and process development of stents used in cardiovascular and cancer treatments (Business Ireland, 2005; IDA Ireland, 2007, 2006; NorDubCo, 2009).

Pharmaceutical TNC plants are concentrated mainly in the GDA and County Cork. The GDA has the largest concentration, with 18 pharmaceutical TNC operations. The Cork region has the second biggest concentration of TNC operations, and the largest single concentration of pharmaceutical TNC activity (26 plants) in Ireland. The third largest concentration, County Galway, has the largest concentration of TNC medical devices facilities (14) in Ireland (IDA Ireland, 2007; InterTradeIreland, 2003; Van Egeraat, 2006).

6.2.5 Irish Government departments and agencies

The Irish Government first identified biotechnology's strategic importance for Ireland's future development in the late 1970s. Yet, in the context of relatively limited STI

initiative developments from the late 1960s onwards, the first public measures to promote biotechnology were formed in the early 1980s, e.g. the National Board for Science and Technology's Programme for Strategic Research (1983) which provided very limited grants for research in selected niche areas, including biotechnology. The first programme to focus specifically on biotechnology was the National Biotechnology Programme (1987), which resulted in the formation of BioResearch Ireland's RIs (Kennedy et al., 1994; Downey, 1979; Senker and Van Zwanenberg, 2000; Morrissey, 2011).

In the wake of the country's first White Paper on Science, Technology and Innovation in 1996, a significant surge in STI and biotechnology-related initiatives occurred. This surge included the development of a variety of Government agency initiatives (detailed further in the following sections), from the late 1990s onwards, which have sought to replicate and develop similar structures as found in the international bio-sector.

Initially, these programmes, i.e. the PRTLI and TFF, focused on addressing the preceding decades of underinvestment in the infrastructures, resources, and skills of the country's PREOs, and the cumulative disadvantages these issues had created, through focusing on developing RIs to facilitate developments throughout the entire bio-sector. Yet, the on-going initiatives have increasingly moved beyond this initial PREO focus towards seeking to develop the conditions that are conducive to creating commercial concerns from PREO-based research, i.e. commercialisation support infrastructures and investor actors. As detailed above, this has resulted in a surge of 'Genentech template' bio-firms (Acheson, and Lambkin, 2009; Department of Trade, Enterprise and Employment, 2006; Government of Ireland, 2007)

As with the international bio-sector, various Government department and agencies oversee specific aspects of biotechnology development in Ireland. The roles and activities of these department and agencies are detailed in the following sections (Burke et al, 2003; Forfás, 2004).

It must be noted that the Irish government and its administration are highly centralised around the GDA, a scenario which has essentially existed since the state's inception, i.e. no clearly defined regional aspects to Irish Government structures, policies or programmes currently exist.

6.2.5.1 The Department of Enterprise, Trade and Innovation

The Department of Enterprise, Trade and Innovation (formerly the Department of Enterprise, Trade and Employment) governs a number of key state agencies, i.e. Forfás, EI, SFI and the IDA Ireland, which implement and realise the department's policies on enterprise, employment promotion, trade development, and the regulation of businesses (The Department of Enterprise, Trade and Employment, 2003).

6.2.5.1.1 Forfás

Established in 1994, Forfás is the national policy and advisory board for enterprise, trade, science, technology and innovation, and both co-ordinates the activities of, and delegates specific powers to, IDA Ireland and EI. Its functions include the provision of analysis, advice and support to the Minister for Enterprise, Trade and Innovation on issues relating to the development of industry, enterprise, technology and innovation. It is also charged with the promotion of scientific research and innovation in association with SFI and the Advisory Council for Science, Technology and Innovation (detailed further below), and is responsible for the publication of Government reports in the areas of scientific research, technological development and innovation (Forfás, 1996; Government of Ireland, 2003; Irish Council for Science Technology and Innovation, 1998; New Economy Strategy, 2003).

6.2.5.1.2 Science Foundation Ireland

SFI was established in 2000 as a sub-board of Forfás through the NDP 2000-2006, with subsequent funding being provided through the NDP 2007-2013. SFI seeks to create a critical mass of world-class research through a competitive research grant scheme, and to facilitate existing Irish enterprises to develop innovation programmes based on indigenous research (Burke et al, 2003; New Economy Strategy, 2003; The ELS Gazette, 2002).

Through the TFF, which represented "...the single biggest investment in research and development in the history of the state" (Department of Trade, Enterprise and Employment, 2001) at its inception, SFI seeks to facilitate PREO-based research developments through attracting internationally renowned researchers into Irish PREOs, as well as developing highly qualified and skilled researchers within Irish PREOs. The TFF ultimately aims to form a critical mass in two key research areas, i.e. biology and biotechnology, and information and communications technology. The fund's target areas within biotechnology are:

- molecular and cellular biosciences,
- bioinformatics & computing,
- functional genomics and proteomics,
- integrative biology, and
- novel enabling technologies from other disciplines (Department of Trade, Enterprise and Employment, 2000; Forfás, 2003; Science Foundation Ireland, 2003).

SFI also seeks to attract new overseas high-technology firms into Ireland so as to foster new indigenous high-tech start-ups, while simultaneously strengthening the capabilities of existing foreign and Irish-owned firms through the advanced opportunities derived from the increased PREO-based activities and capabilities (Technology Ireland, 2004; Government of Ireland, 2003).

6.2.5.1.3 The Industrial Development Agency Ireland

The Industrial Development Agency Ireland (the IDA) was established in 1949 to take responsibility of Ireland's industrial development. Its functions have changed over the decades, reflecting the evolving nature of Ireland's industrial policy. Since 1993, it has been responsible for securing new overseas investment from high-tech, manufacturing and international services sectors (such as the electronics, pharmaceuticals and healthcare, and international financial services sectors), and encouraging the expansion of existing Irish-based FDI enterprises and operations. The IDA seeks to attract international projects which can operate competitively and profitably from within Ireland, and to embed TNC R&D operations through engendering research networks with PREO and commercial actors. In 2008, it was directly responsible for the creation of over 8,000 new jobs, while IDA assisted companies employed over 136,000 people in permanent employment, and spent over €16 billion in the Irish economy (IDA Ireland, 2003, 2004; The ELS Gazette, 2002; Department of Trade, Enterprise and Employment, 2009; New Economy Strategy, 2003).

The IDA offers several incentives to TNCs to locate stand-alone R&D operations in Ireland, to add R&D activities to their existing operations, or to expand their existing R&D activities. These incentives include:

- The R&D Capability Grant Scheme, to assist TNCs expand or establish new R&D operations. Among the scheme’s incentives are capital cost contributions

towards establishing R&D units,

- A multi-faceted R&D funding programme that offers TNCs feasibility studies on planned R&D programmes, training to increase basic skill levels of staff and management, and a pilot R&D project to identify potential strengths and weaknesses so as to enhance their R&D activities,
- The Research Technology & Innovation scheme, to encourage TNCs to develop existing Irish-based R&D activities, or form new R&D projects. The initiatives funding is capped at €650,000, which can be applied to either product or process development activities, and
- The Innovation Partnership Initiative, which is run in collaboration with EI. This provides financial assistance to develop collaborative research projects with Irish PREOs, including IoTs (Enterprise Ireland, 2006; IDA Ireland, 2007).

The IDA also offers R&D supports to drive research developments across industrial sectors:

- R&D Tax Credits: introduced in 2004, these aim to encourage firms to undertake additional and/or new R&D activities, and to engender research alliances with PREOs by requiring recipient firms to outsource up to 5% of total R&D expenditure to an EU-based university. This is facilitated by allowing firms avoid paying tax on earnings from IP where the underlying R&D was conducted in Ireland. The credits apply to research related overheads, plant/machinery, wages and buildings, and
- Stamp Duty on IP: in order to attract IP to Ireland, no stamp duty tax is charged on IP transfers into the country, including any patent, trademark, copyright, registered design, or invention transfers (IDA Ireland, 2007).

6.2.5.1.4 Enterprise Ireland

Enterprise Ireland (EI) was established in 1996, and is responsible for the development of indigenous industry. Its key functions include the provision of a wide range of business supports and funding to indigenous firms so as to establish a competitive position in the global marketplace and to embed FDI operations in the Irish economy. Several of EI's business supports focus specifically on biotechnology, including the hosting of the BiotechnologyIreland website (Burke et al, 2003; The ELS Gazette, 2002; Treacy, 1998).

EI seeks to orientate the indigenous bio-sector towards a more commercial direction through its biotechnology strategy. The strategy aims to facilitate and nurture 'Genentech Template' style start-up bio-firm developments through developing indigenous private sector seed and VC funds, and seeks to encourage foreign entrepreneurs and early stage companies with sufficient development potential to locate in Ireland (New Economy Strategy, 2003).

EI has also developed several schemes and incentives to address weaknesses in the management and protection of indigenously generated IP. These developments mirror entrepreneurial supports present in the leading international bio-sectors. Two codes of practice relating to the management of IP generated through PREO-based research activities have been developed, i.e. the IP Fund for the Higher Education Sector, and the IP Assistance Scheme.

The IP fund seeks to address the exorbitant costs and complexities associated with licensing which can undermine PREO-based licensing developments. Patent filing can cost €7,000 for the first year, following which a patent co-operation treaty (PCT) must be sought, costing another €7,000. A PCT lasts for 18 months and applies to 120 countries, yet if an academic wishes to maintain the patent (for example, where an academic hasn't yet licensed the product/process, or a collaborating company refuses to take on the patenting costs), applications must be made in individual countries, at which point costs approach €50,000. EI's patenting fund will only finance this process if a technology displays sufficient commercial potential to justify the investment (The Department of Enterprise, Trade and Employment, 2008; World Intellectual Property Organization, 2007).

The IP Assistance Scheme, established in 1998, provides information and advice on the protection, development and commercialisation of IP. The receipt of funding for the legal protection of IP depends on the strength of a patent application, which must include detailed marketing and manufacturing plans (Forfás, 2004; The World Intellectual Property Organization, 2007).

EI also hosts an Innovation Partnership initiative scheme to support joint industry-PREO research through providing financial, business advice and structural supports to the relevant actors. The scheme seeks to open new business possibilities for Irish

researchers. Additionally, EI has introduced a commercialisation fund to support the commercialisation of PREO-based research that displays clear commercial potential in the areas of Life Sciences/Biotechnology, Informatics, and Industrial Technologies. This fund focuses on start-up developments, yet also seeks the development of technologies "...that can be licensed to an in-house company or to an existing Irish company. Otherwise, [EI looks] at licensing to an international or multinational company" (Technology Ireland, 2004: 29). To optimise licensing efforts, the fund includes a proof-of-concept grant that allows PREO researchers to develop a product prototype from commercially viable research over a three year period so as to gain a better response from firms (Enterprise Ireland, 2007, 2005; Forfás, 2004).

6.2.5.1.5 Enterprise Ireland's Bioresearch Directorate

EI took control of BioResearch Ireland in 2003 as part of its biotechnology strategy, creating the EIBD. Under the stewardship of EIBD, the original research orientation of BioResearch Ireland's RIs has been augmented to include a more pronounced commercial emphasis to their activities. This reflects the aim of EI's biotechnology strategy, i.e. to increase the commercialisation of PREO research through technology transfers and the development of campus-based initiatives related to RI's research activities (BiotechnologyIreland, 2005; Burke et al, 2003).

6.2.5.1.6 The Advisory Council for Science, Technology and Innovation

The Advisory Council for Science, Technology and Innovation (ACSTI) was established in May 2005, replacing The Irish Council for Science, Technology and Innovation. ACSTI is an independent government advisory council, supported by Forfás, that answers directly to the Minister for Enterprise, Trade and Innovation. It provides advice to the Minister on policy-related issues relating to STI through compiling detailed reports (Burke et al, 2003; The Advisory Council for Science, Technology and Innovation, 2006).

6.2.5.2 The Department of Education and Skills

The Department of Education and Skills supervises the country's PREOs, directly influencing their under-graduate and post-graduate educational biotechnology programmes. The department aims to develop and promote education programmes relevant to the social, cultural and economic needs of the country (The Department of Education and Science, 2007).

6.2.5.2.1 The Higher Education Authority and the Programme for Research in Third Level Institutions

The Higher Education Authority (HEA) is the statutory planning and developmental body for higher education and research in Ireland. It is the funding authority for the PREOs and a number of designated higher education institutions, such as the Royal College of Surgeons, Ireland. As such, it is the main source of funding for third and fourth level education in biotechnology and related disciplines in Ireland. In addition, the HEA administers the Programme for Research in Third Level Institution (PRTLI), which was established in 1998 to fund science and technology research in these education institutions (Government of Ireland, 2003; Higher Education Authority, 2005).

The PRTLI targets the development of the research capabilities of the country's PREOs through infrastructural and programme investments designed to support inter-disciplinary and inter-institutional research. The PRTLI has been central in the indigenous bio-sector's on-going developments, funding the establishment of 28 biotechnology/biotechnology-related PREO-based RIs since its introduction. Under cycle 4 of the PRTLI (2007-2011), announced in January 2007, an additional €190 million will be invested in research (Forfás, 2004; HEA, 2006, 2007b).

6.2.5.3 The Department of Agriculture and Food

The Department of Agriculture and Food monitors and controls aspects of food safety and animal and plant health, and regulates the agriculture and food industries through the implementation of national and EU legislation. The Department also supervises several state bodies engaged in research, training, market development and promotion in the agriculture and food sectors (The Department of Agriculture and Food, 2006).

6.2.5.3.1 Teagasc

Teagasc, the Irish agriculture and food development authority, was established in 1988 through the merger of two Government agencies, An Foras Talúntais (formerly responsible for agricultural research) and An Chomhairle Oiliúna Talmhaíochta (formerly responsible for agricultural education and advisory services). Teagasc is a semi-state agency that is responsible for R&D, training and advisory services in the agri-food sector. It runs nine dedicated RI's throughout Ireland, five of which (Figure 6.2) are engaged in biotechnology-related research activities (Teagasc, 2005, 2006).

6.2.5.4 The Department of the Environment, Heritage and Local Government

The Department of Environment, Heritage and Local Government has a very wide

remit. It is responsible for the promotion of sustainable development, the protection of the country's environment and heritage, infrastructure provision, regional development and local government. It is also responsible for the administration of governmental policy on Genetically Modified Organisms (GMOs) through the Environmental Protection Agency (EPA) (The Department of the Environment, Heritage and Local Government, 2006).

6.2.5.4.1 The Environmental Protection Agency

The EPA was established in 1993 with the remit of protecting the Irish environment. It supervises the government's GMO regulations, which are regulated under two EU Directives, i.e. directive 90/219/EEC, on the use of GMOs in Europe, and directive 2001/18/EC, on the introduction of GMOs into the Irish environment. The EPA also maintains a publicly accessible database on GMO users in Ireland.

The EPA provides research funding for biotechnology-related projects, including projects which evaluate the effects and impacts of GMOs on Ireland's biodiversity. Additional EPA sponsored programmes include the advanced technologies for environmental protection programme, and the Science, Technology, Research & Innovation for the Environment programme. These seek to utilise nanotechnology and biotechnology in developing new solutions to environmental problems (The Department of the Environment, Heritage and Local Government, 2006; The Environmental Protection Agency, 2004, 2007a, 2007b).

6.2.5.5 The Department of Health and Children

The Department of Health and Children is responsible for the strategic planning and implementation of policies related to the Irish health system, in conjunction with the Health Service Executive (HSE). The Department formulates policy through an evidence-based approach, overseeing the activities of the Health Research Board (HRB) and RH research laboratories (as detailed above) (The Department of Health and Children, 2007, 2008).

The HSE was established in 2005 to manage the delivery of the healthcare and personal social service in Ireland. It replaced the previous regional Health Boards and Authorities by merging their activities into a single national entity. The Minister for Health and Children has overall responsibility for the HSE in Government (Health Service Executive, 2009).

The HRB was established in 1986 to improve health through research-based initiatives. The HRB supports a wide variety of medical research on medical and health-related activities, including child health, drug misuse, and mental health issues. The findings from these programmes assist Government policy formulation (The Health Research Board, 2006a, 2006b).

The HRB supports various biotechnology-related research facilities and programmes, including biomedical research fellowships and the development of clinical trial facilities, in collaboration with the Dublin Molecular Medicine Centre (DMMC), based in several Dublin-based RHs under the Dublin Centre for Clinical Research banner (Dublin Molecular Medicine Centre, 2006).

6.2.6 Additional actor types

6.2.6.1 Suppliers of Goods and Services

Due to the limited nature of the Irish bio-sector's activities, prior to the introduction of the on-going Government initiatives in the late 1990s, supply actor developments were limited. This meant that the main markets for Irish supply actors were in European markets, in particular the United Kingdom bio-sector.

Despite the on-going sectoral initiatives, the number of specialist supply firms in the bio-sector remains limited due to the continuing low levels of sectoral commercial and research activities. Indeed, many sectoral service requirements, such as specialist business development services and patenting information, are predominantly provided by government agencies, such as EI. This means that a significant proportion of supply firm business remains with non-Irish contacts (BiotechnologyIreland, 2007; Cato Research, 2007).

It must be noted that the review of sectoral actors found that the majority of the bio-sector's supply firms are located in the GDA.

6.2.6.2 Sub-national Biotechnology Centres

No biotechnology centres exist in the Irish bio-sector. Existing research may display a regional focus, e.g. the RIs under the stewardship of EIBD, yet this is due to the locations of their host universities, not because of specific or premeditated policy decisions on locating research groupings in, or at county level centres. Sub-national government is poorly developed as the Irish government's structure and administration is highly centralised around the GDA, i.e. regional-level government structures are non-

existent, while county and city councils have a very limited range of functions and powers.

6.2.6.3 Trade Associations

There are several trade associations in the Irish bio-sector, yet these are solely post-initiative developments.

6.2.6.3.1 InterTradeIreland

InterTradeIreland is one of six North/South implementation bodies established in 2000 under the control of the North/South Ministerial Council created as part of the Belfast Agreement in 1998. It seeks to engender business development networks, co-ordinate trade, and facilitate information exchanges between the two administrations on the island of Ireland. This body has published many cross-border sectoral reports, including *Mapping the Bio-island* (2003) (as detailed in chapter 4) (Irish Venture Capital Association, 2003).

InterTradeIreland has proactively supported cross-border initiatives to encourage the development of the bio-sectors on the entire island, and has launched research and network-based partnerships to develop business networks between various actors in Ireland and the UK. These include:

- Fusion: a technology transfer programme to establish PREO/business collaborations,
- INNOVA: a collaborative R&D programme that funds research collaborations between PREOs and private companies, particularly Small to Medium Enterprises,
- Expertiseireland.com: an on-line research commercialisation networking portal which acts as a research database that allows researchers advertise their commercially orientated research activities to interested firms, and
- BioMedIreland: a networking organisation that facilitates knowledge-based network developments between health technology and biotechnology researchers. It was formed by InterTradeIreland, the Irish Medical Devices Association, BioBusiness Northern Ireland and the Irish BioIndustry Association (InterTradeIreland, 2006; Government of Ireland, 2003; InterTradeIreland, 2006).

6.2.6.3.2 The Irish BioIndustry Association

The Irish BioIndustry Association (IBIA) was established in Dublin by the Irish Businesses and Employers Confederation (IBEC) in 1998 to promote the development of the indigenous bio-sector, particularly in areas influencing the commercialisation of research. The IBIA engages in a wide range of activities, including government lobbying to create a more supportive regulatory environment and optimise government support for the bio-sector's development. The IBIA actively promotes the development of the PREO educational and research infrastructures, and seeks to increase the level of networking and R&D collaborations between its members and PREOs through working groups and private actor centred information dissemination services (The Irish BioIndustry Association, 2007; The Irish Scientist, 1999; Technology Ireland, 2004).

6.2.6.3.3 Bioconnect Ireland

Bioconnect Ireland is a voluntary organisation that was established in 2001 by bio-sector actors returning to Ireland from various overseas locations in response to the significant issues they experienced in accessing information on the various sectoral activities which had developed in their absence. As such, an informal networking forum was established where sectoral actors could meet to discuss current activities and issues. Due to its success, similar organisations have been established internationally (discussed below) (Enterprise Ireland, 2007; National Institute for Bioprocessing Research and Training, 2007).

6.2.6.3.4 Biolink USA-Ireland

Biolink USA-Ireland was formed in 2003 to facilitate linkage developments between expatriate US-based and Irish sectoral actors. The organisation has chapters (regional focal points) in 10 US biotechnology centres, including Boston, Chicago, New Jersey, New York, North Carolina, Philadelphia, San Diego, San Francisco, Texas, and Washington DC (Biolink USA-Ireland, 2005; BiotechnologyIreland, 2005a).

6.2.6.3.5 Biolink Canada-Ireland

Biolink Canada-Ireland was created in 2006 in collaboration with EI in response to the success of Biolink USA-Ireland, to facilitate the development of linkages between actors in academia, commercial enterprises, and government agencies located in Ireland and Canada, for the benefit of both bio-sectors (Biolink Canada-Ireland, 2006; Enterprise Ireland, 2007b).

6.2.6.3.6 TechLink UK-Ireland

TechLink UK-Ireland was established in 2003 to establish networks among expatriate

Irish professionals working in the UK in the areas of biotechnology, nanotechnology, pharmaceuticals, academia and services (BiotechnologyIreland, 2005b; TechLink UK-Ireland, 2007).

6.2.6.4 Private Research Institutes

There are presently no private Irish biotechnology orientated RIs in the Irish bio-sector, while very limited non-Irish private RI activities have occurred. For example, the Wellcome Trust has invested in several RI- and RH-based developments since the late 1990s, such as Dublin City University's Vascular Health Research Centre and University College Dublin's Conway Institute of Biomolecular and Biomedical Research (Department of Enterprise, Trade and Employment, 2006; DCU, 2005).

6.2.6.5 Repositories (Gene Banks)

No repository/gene bank developments have occurred in Ireland. An all-Ireland gene bank, GeneLibrary Ireland, was jointly proposed in 2003 by the HRB and the Northern Ireland Research and Development Office so as to develop a research resource that would be used in combination with the Human Genome project. The library is still in the planning phase, and is intended to consist of a bank of anonymous DNA samples drawn from a cross-sectional sample population, linked to clinical and demographic data (Health Research Board, 2005, 2009).

6.3 DISCUSSION

All actor types are important as incubators or transfer mechanisms within the bio-sector's complex Post-Fordist sectoral value chain. The bio-sector’s innovation process can be characterised as a complex inter-linked innovation system which involves PREO-based actors seeking to develop and exploit commercially viable research findings, bio-firms (through VC/investor actor assistance) transferring PREO derived research results/findings to the market place through applied research programmes, and TNCs, which seek to facilitate such commercial developments so as to fill their product development pipelines.

These activities are supported and facilitated by various Government department and agency initiatives and policies which seek to engender commercially viable PREO research activities and downstream transfers, so as to optimise bio-firm developments through commercial development supports, resources and infrastructures, and create a positive and supportive policy environment. Additionally, the bio-sector's innovation process is supported and facilitated by the activities of dedicated specialist goods and

service suppliers, trade associations, and sub-national biotechnology centres (Boje, 2001; Harrison, 1997; Owen-Smith and Powell, 2007; Barley et al., 1992; Malecki, 1997).

The development of the Irish bio-sector has occurred over two distinct epochs, i.e. the pre- and post-initiative eras, which have had considerable impacts on the structures and activities of the bio-sector's actors.

The indigenous bio-sector first emerged in the early 1980s following the introduction of the first government sponsored biotechnology programmes, including the NBP. Yet in the context of the preceding long-term absence of investments in the research capabilities, infrastructures and resources of the country's PREOs, and the virtual absence of dedicated commercialisation support infrastructures to support indigenous industrial developments in the wider economy, the pre-initiative bio-sector's development trajectory, activities, capabilities and resources were very limited.

The restricted nature of the pre-initiative PREOs meant little commercially viable research developed. In combination with the virtual absence of commercial supports, particularly the substantial investor actor limitations, a very small number of pre-initiative bio-firm developments occurred, mainly in platform related areas derived predominantly from non-Irish IP sources. Paradoxically, the limited sectoral activity undermined the development of sectoral support actors, whose restricted nature undermined potential sectoral developments by reinforcing the conservative (platform) nature of existing bio-firms, which fed into the limited level of PREO-based innovative activity (Morrissey, 2011).

The poor innovative nature of the pre-initiative bio-firms links into national trends in the Irish industrial base during this period. From independence up until the late 1950s, the Governments' STI and industrial policies focused on the country's agricultural and food sectors, which contributed to and compounded the negligible role innovative research had in indigenous industry. Yet Irish industry at that time had little need or motivation to innovate due to decades of tariff protection, while limited market size/demands meant they were mainly small in scale, and engaged in short production runs of low quality designed products. Despite relatively modest increases in PREO-based research occurring from the late 1960s onwards, indigenous firms could not

benefit from these developments due to their low research activities and capabilities, i.e. an innovation paradox existed (Cooper and Whelan, 1973; Teavey, 1995; Morrissey, 2011).

Despite changes to the Government's industry policy from the late 1950s onwards, i.e. the adoption of open market policies to proactively seek FDI, and Ireland joining the European Economic Community (the forerunner to the European Union) in 1973, little emphasis was placed on facilitating changes to the nature and character of the indigenous industrial base up until the mid 1990s. This was despite several Government sponsored reports from the early 1980s onwards calling for such measures to be introduced (Acheson, and Lambkin, 2009; Teavey, 1995).

TNC FDI operations which located in Ireland following the adoption of the open market policies were typically engaged in low skilled, low wage assembly line production to serve the UK and continental European markets. They formed, at their most basic level of operations, very few linkages with the Irish economy. In relation to the Irish-based pharmaceutical TNC operations established during this period, their branch plant nature meant they conducted little research activities, which further undermined potential PREO- and firm-based innovative developments in the indigenous bio-sector (Cogan and McDevitt, 2000; National Economics and Social Council, 1982).

Overall, these issues reflected a lack of coordination between the Government's STI and industrial policy strands, i.e. industrial policies did not seek to engender commercial developments which linked into PREO research, while indigenous spin-off or start-up developments were undermined by a poorly developed and constructed policy environment which failed to drive and/or facilitate indigenous entrepreneurial and/or innovative developments, thus establishing the innovative paradox in the indigenous industrial base (Morrissey, 2011).

An additional policy-related issue which undermined the bio-sector's optimal development was the established policy emphasis of promoting individual industrial sectors through individual firm development/cultivation, i.e. there was an absence of defined regional aspects to Irish Government structures, policies or programmes from the state's inception until 2002.

Observable regional differences existed in how the indigenous bio-sector developed, due to different regional endowments of sectoral actors. Three main pre-initiative sectoral concentrations had emerged by the late 1990s, as detailed in Table 6.3.

Table 6.3: Regional endowments of pre-initiative sectoral actors	
The Greater Dublin Area (the GDA)	- Bio-firms: 16. - PREOs: 26 (five universities, three IoTs and 18 RIs, including three BioResearch Ireland RIs). - Largest concentration of TNC activities.
The Cork City area	- Bio-firms: 8. - PREOs: 4 (one university, one IT, and 2 RIs). - Second largest concentration of TNC operations, largest pharmaceutical TNC activity concentration.
The Galway City area	- Bio-firms: 5. - PREOs: 4 (one university, one IT, and 2 RIs). - Largest concentration of TNC medical devices facilities.

Based on (InterTradeIreland, 2003; Enterprise Ireland, 2005; IDA Ireland, 2007; van Egeraat and O'Byrne, 2010).

Due to its greater actor endowment, the GDA attracted a larger share of the pre-initiative resources and funds allocated under the restricted Government initiatives. This meant that the GDA enjoyed cumulative advantages in comparison to other areas of the sector, in particular the Cork and Galway city areas. Regional imbalances, in terms of development trajectories, resource and actor allocations, undermined the development of these regions, as skills and resources migrated to the relatively more asset rich GDA. Regional differences became entrenched, which undermined sectoral developments nationally.

The introduction of on-going public actor initiatives seeking to develop the indigenous bio-sector, introduced since the late 1990s, have led to rapid and significant sectoral developments, relative to conditions and activities of the pre-initiative bio-sector. Their initial focus on developing the research capabilities of the country's PREOs has created significant infrastructures, specifically the new RI developments, resources and skills which have advanced the range and depth of their research activities.

The subsequent introduction of dedicated commercialisation supports and infrastructures, particularly the development of dedicated public VC funds to address the bio-sector's chronic investor actor weaknesses, have facilitated the emergence of post-initiative start-up bio-firms, which mirror the international bio-sector's 'Genentech template'.

However the ultimate impact of these initiatives on the bio-sector has been limited for a

variety of reasons:

- the initiatives have had to address the substantial long-term cumulative weaknesses in the PREOs and commercialisation supports by introducing and developing missing infrastructures, resources and skills,
- significant commercial results have yet to materialise in the bio-sector due to the on-going compromised nature of the pre-initiative bio-firms, i.e. the development initiatives have essentially by-passed these bio-firms, and as the post-initiative bio-firms have yet to produce significant levels of commercial products and/or processes,
- the bio-sector's activities are predominately driven and facilitated by/through public actor activities, i.e. limited private actor developments have occurred, which restricts its commercial orientation,
- the nature and character of entrepreneurial and innovative developments are being restricted by the narrow range of commercialisation supports, i.e. the general absence of alternative investor actors outside of public funded VCs,
- downstream commercial avenues for indigenous actors' remain limited, particularly in relation to TNCs. Despite on-going international structural development trends among TNCs being reflected in Irish-based TNC operations, their activities remain predominantly manufacturing orientated/branch plant in nature, and
- the limited level of downstream sectoral activity also means that limited goods and service supplier development have occurred.

Essentially, the Irish bio-sector's development has been disjointed and it continues to experience 'cumulative disadvantages' due to the lack of coordination between the Government's STI and Industry policy strands. This is reflected in on-going trends in the wider Irish industrial base. Outside of the biotechnology and NICT sectors, little policy emphasis has been placed on facilitating or driving indigenous industrial developments, i.e. industrial policies still focus on attracting TNC FDI, or in addressing the on-going research and innovative limitations of Irish firms. These issues mean that an innovation paradox remains in the indigenous industrial base.

Additionally, no defined regional aspects emerged in Irish Government structures, policies or programmes until 2002, when the National Spatial Strategy (NSS) was

introduced. The NSS was a long-term strategic vision for Ireland's future spatial development that indistinctly detailed an overreaching national framework for balanced regional development for the various policies and programmes of the relevant government departments and agencies. However, the funding for the central component of the NSS has been deferred since 2008 (The Stationery Office, 2002).

Despite the NSS creating a national framework for balanced regional development, no regional elements were/have been introduced to the on-going sectoral development initiatives. As such, no effort has been made to address the deepening regional differences in how the indigenous bio-sector has developed. Table 6.4 presents a comparison of pre- and post-initiative regional endowments of sectoral actors (no significant changes of TNC endowments have occurred beyond those detailed in section 6.2.4).

Table 6.4: Comparison of pre- and post-initiative regional endowments of sectoral actors

	Pre-initiative actor endowments	Post-initiative actor endowments
The GDA	- Bio-firms: 16. - PREOs: 26 (five universities, three IoTs and 18 RIs).	- Bio-firms: 28. - PREOs: 34 (five universities, three IoTs and 26 RIs), - The overwhelming majority of the country's VC firms.
The Cork City area	- Bio-firms: 8. - PREOs: 4 (one university, one IT, and 2 RIs).	- Bio-firms: 13. - PREOs: 9 (one university, one IT, and 7 RIs).
The Galway City area	- Bio-firms: 5. - PREOs: 4 (one university, one IT, and 2 RIs).	- Bio-firms: 7. - PREOs: 7 (one university, one IT, and five RIs).

Based on (Enterprise Ireland, 2005; IDA Ireland, 2007; van Egeraat and O'Byrne, 2010).

Due to the absence of regional development elements to Government policies, the bio-sector's activities remain heavily focused on the GDA and the Cork and Galway city areas due to their larger actor and activity concentrations. Smaller centres have emerged in other areas of the country located around PREOs, i.e. IoTs, yet have few bio-firms and/or no TNC operations located in close proximity to them meaning their activities are limited in scale and scope. Essentially, despite increases in the activities of all PREOs, and in sectoral activities nationally, the Government's uniform policy approach to the sector's development continues to entrench existing regional differences, i.e. skills and resources continue to migrate to the more asset rich GDA, undermining sectoral developments nationally (Chen at al., 2011).

Overall, the review of the Irish bio-sector's actors shows that, when compared with the

international bio-sector's template, there are nine identifiable actor types in the indigenous bio-sector. Ireland currently has no county level biotechnology centres, private RIs, or genetic repositories/gene banks. Sectoral activity is mainly concentrated in the 'upstream' end of the sector's evolving value chain, and is spatially concentrated in three main urban locations, in particular the GDA.

The following chapter analyses the informal and formal networks found between the actors detailed in this chapter.

CHAPTER 7:
FORMAL AND INFORMAL INTER-ACTOR NETWORKS IN THE INDIGENOUS BIOTECHNOLOGY SECTOR

7.1 INTRODUCTION

Two epochs can be identified in the indigenous biotechnology sector's (bio-sector) development, relative to the introduction of the on-going government development initiatives in the late 1990s. The pre-initiative sector was characterised by limited sectoral actor numbers, limited sectoral activities, and a general absence of sectoral development supports. In contrast, the bio-sector has undergone substantial developments due to the on-going public initiatives having primarily focused on engendering and exploiting PREO-based commercial developments in order to drive the bio-sector's activities.

This chapter analyses the formal and informal inter-actor networking arrangements found in the bio-sector's value chain during both epochs. This analysis is based on the findings generated from the biotechnology firm (bio-firm) surveys and sectoral actor interviews, and the review of the indigenous sector actor types. These networking arrangements are compared and discussed in relation to the bio-sector networking template in order to present an overview of the indigenous bio-sector's network structure and development. Additionally, this chapter draws from chapter 5, so as to place the development of the bio-sector's networks in their proper policy and economic development contexts.

The chapter is divided into two sections. Section one compares the formal and informal networking arrangements of the Irish bio-sector's actors as found in both the pre- and post-initiative bio-sectors to the international bio-sector's network typologies. Section two presents a discussion on the indigenous bio-sector's network structure, and analyses the development and evolving nature of the bio-sector's network arrangements and their regional characteristics.

7.2 INTER-ACTOR NETWORKS IN THE INDIGENOUS BIO-SECTOR

Regional differences in sectoral actor endowments, and the institutional and non-institutional characteristics of these actors, mean that significant differences exist in how bio-sector value chains are constructed, i.e. regional specific organisational forms impact on how inter-actor networks form, function, and develop.

The innovation process in the hub bio-sectors can be characterised as a tripartite value chain formed around the coordinated efforts of three principal actors, i.e. Public Research and Education Organisations (PREOs), bio-firms, and pharmaceutical Transnational Corporations (TNCs). These actors create a complex non-linear, continuously networked interactive structure. Bio-firms are the linchpin in the bio-sector's innovation process as they occupy the middle rung in the industry's value chain. Two broad activity categories, relative to a bio-firm's position in the innovation process, can be characterised:

- upstream sectoral activities, i.e. research-based activities, which are predominantly orientated around the activities of PREOs, and
- downstream sectoral activities, i.e. the developmental stages of the clinical trials process, traditionally the domain of TNCs, and the final sale to the consumer (Malecki, 1997; Owen-Smith and Powell, 2007; Stuart et al., 2007; Giesecke, 2000).

7.2.1 PREO-based research networks

The bio-sector's innovation process begins with PREO-based scientists engaging in collaborative and exploratory basic research programmes. These collaborations are characterised by informal, strategic, exploratory, and exploitative networks that involve exchanges of filtered tacit and codified scientific and technical competences, skills, and research-related equipment and resources. Such networks develop through the under-graduate and post-graduate and professional careers of academics, as well as through industrial and/or PREO work placements, publications, and conference presentations (Malecki, 1997; Owen-Smith and Powell, 2008; Prevezer and Swann, 1996; Lia and Gengb, 2012).

The organisational structures and research capabilities of PREOs depend on their place specific research communities and infrastructures. These represent idiosyncratic and localised knowledge fields of researcher specific tacit knowledge, which determine the effectiveness of the filtering aspect of networks, and also how academics interact with, and assume non-local skills and knowledge (Owen-Smith and Powell, 2008; Gertler and Levitte, 2005; Prevezer and Swann, 1996; Engel and Del-Palacio, 2011; Lee, 2012).

The level of PREO-based research activity in the pre-initiative Irish bio-sector was constrained by decades of public actor under-investment in PREO infrastructures,

facilities, equipment and skills. Of the four PREO actor types:

- the biotechnology/biotechnology-related university departments were, relatively, the most developed of the PREO actors;
- a very limited number of research institutes (RIs) were formed during the 1980s, in particular BioResearch Ireland RIs;
- hospital-based research was virtually non-existent due to the near absence of research facilities, and;
- IT-based research was essentially non-existent due to their historic focus on the application of technology rather than its development.

Very limited cross-institutional networks developed due to the presence of extensive structural inflexibilities, i.e. the PREO actors were clearly differentiated, and limited intra- or inter-institutional collaboration occurred due to institutional inertia. Respondents commented that where alliances did form, they were mainly intra-departmental in nature, as cross-institutional network developments were undermined by the lack of common research infrastructures, i.e. academics accessed different technologies, and/or had different but incompatible experiences of similar/related technologies. One university-based academic commented:

> "...within my Department, we could collaborate a bit where we could. But when you talk about linking up with researchers in other universities, we simply couldn't. Even where obvious projects could have been developed, we just couldn't do it. The gaps in what we had, what we could do, on both sides, the logistics of it all was just too great" (University respondent 4, interview).

In combination, these issues heavily restricted the levels of scientific tacit and codified knowledge academics could generate.

Due to the limited research capabilities and activities of the PREOs, many academics established alliances with non-Irish researchers, predominantly US- and UK-based academic and commercial actor-based researchers, i.e. they sought to develop alternative forms of proximity in order to access more substantial resources and information sources. One University-based academic commented that:

> "getting in contact with [bio-]firms was tough, very often they would get in touch with us. But most of these developments [with university- and/or commercial actor-based researchers] came mainly through old contacts we had with former students or colleagues that had left for jobs in other countries" (University respondent, interview).

However, the nature of these developments was constricted by the limited activities and

capabilities of the Irish researchers. A university-based respondent commented that while Irish academics "could sometimes access better equipment, and sometimes slightly larger funds [through these alliances] than we'd normally be able to get...[the alliances were restricted] by what we could offer at the time. Which wasn't all that much" (University respondent 2, interview). Furthermore, the high management costs of these alliances meant such alliances were predominantly formal in nature, which undermined spillover developments.

Significant and sustained developments have occurred in the PREOs since the late 1990s due to on-going development initiatives. PREO interview correspondents stated that the Programme for Research in Third Level Institution (PRTLI) and Science Foundation Ireland's (SFI) Technology Foresight Fund (TFF) programmes, specifically, have addressed many serious infrastructural, facility, personnel, and equipment issues which had previously restricted PREO-based research activities. Overall, "a research community has been built from the ground up [due to these initiatives], this is taking time to bed in" (Academic respondent 5, interview).

The PRTLI investments have introduced common infrastructures between the different institutions, a crucial development, as "you have to have some sort of common technology platforms, an interface between the different scientists, to allow inter-institutional collab[oration]s" (RI respondent 5, interview). As such, the level of internally generated tacit and codified research knowledge has surged, which has facilitated significant increases in intra- and inter-institutional exchanges of personnel, competences and resources through strategic, economic, exploratory and exploitative networks, and has also advanced collaborative alliances with non-Irish academics.

Many interview respondents commented that the most important of the various PREO-based developments has been the establishment of the new RIs through the PRTLI. One University respondent commented:

> "The research centres have transformed the research landscape. It's day and night stuff really, with regards to what was there and what we have now. Real money has been pumped into developing them...you now have access to new equipment, skills, resources at a level we could only have dreamed about in the past" (University respondent 7, interview).

The RIs have been established in close proximity to their 'parent' universities, and have been specifically established as inter-departmental and/or inter-university institutions,

i.e. their structures have pronounced collaborative elements, and they also have a defined commercial orientation. A public development agency respondent summed up the attraction of RIs for the government:

> "...the Government quite likes the idea of this joining together of minds, and they view these centres as a very cost effective way of spending money. You are asking people to set up some infrastructure that would be shared across different institutions" (Government agency respondent 2, interview).

Indeed, relative to the pre-initiative RIs, these new institutes have facilitated more extensive research collaborations and intra- and inter-department, and inter-institutional network developments between the RIs and their 'parent' universities. However, the overall development of collaborative alliances between the RIs is ultimately restricted by their different and specific research foci, i.e. extensive collaborative preliminary laboratory work does occur between certain RIs, it is limited to instances where research areas overlap. Limited information exchanges and personnel transfers have also occurred for the same reason.

Additionally, due to the RI centred focus of the on-going development initiatives, Hospital- and IT-based research activities remain limited. In part, this is due to their relatively more entrenched infrastructural and skills weaknesses having taken longer to address. However, many interview respondents highlighted the establishment of the Dublin Molecular Medicine Centre (DMMC) as being a crucial development in the Irish bio-sector. The centre's cross-institutional structure has facilitated significant informal, tacit information exchanges through the sharing of key personnel among its members, including research nurses and several post-doctorate researchers.

Overall, the post-initiative PREO actor and network developments have produced positive externalities and have facilitated limited spillover developments. The PRTLI's funding means that academics now have access to up-to-date equipment, which has allowed them to internalise more research and reduce their dependence on non-Irish RIs. This has mitigated certain issues, particularly timetable issues, and means academics can commit to a wider range of research topics through optimising their activities. Several respondents noted that access to modern, up-to-date equipment is vital in order to gain international recognition:

> "...in order to get papers published...you have to have used certain techniques. This means there is a certain element of keeping up with the Joneses in order to keep a presence, in order to bring in funding. This is a serious point, as you can't get your work

> recognised [internationally] if you are stuck using old practices or procedures. If you're not seen as being up to date, you simply can't progress" (RI respondent 4, interview).

This has impacted on the non-local linkages formed by Irish researchers. Indigenous researchers are increasingly able to 'advertise' their activities internationally and develop networks with non-Irish researchers. These developments are allowing Irish academics to access international knowledge networks, and deepen and more optimally exploit the various pre-initiative linkages they developed with non-local academics.

In alliance with the cross-institutional nature of the RIs, the increased level of research activity resulting from the infrastructural developments has also driven network density:

> "The most obvious example I know of sharing of infrastructure and of know-how is a cohort of [Irish] researchers in an area that was new to us. We didn't see that one developing, but they have been absolutely critical in developing the [existing] programme between the different players [in the RI], as well as the new activities" (RI respondent 8, interview).

The size and scale of the PRTLI and SFI, relative to pre-initiative investments, have also created a PREO-centred 'brand', which has engendered a series of cumulative benefits. This 'brand' has advertised the improved resources and capabilities of Irish academics internationally, facilitated improved access to international knowledge networks, and has allowed Irish academics to deepen and more optimally exploit the various pre-initiative linkages they had developed with non-Irish academics.

Additionally, supporting and facilitating these developments has been the attraction of high skilled, internationally renowned 'star' researchers into Ireland through SFI's TFF. One academic respondent commented that the TFF:

> "...has really worked. The type of academic it has attracted is high quality...these guys, the first wave if you like, have spread the word back in their home countries, about what's happening here, about our activities and what we can do. That's opened a lot of doors for us. Really, it [the TFF] has built on its success in lots of different ways" (PREO respondent 3, interview).

Regional endowment of researchers determines the effectiveness of the filtering aspect of networks in localised learning processes, i.e. how the local research 'buzz' is augmented by researchers accessing codified knowledge from non-local sources. Significant non-Irish research expertise have been imported into Irish PREOs, which has both facilitated improved access to international knowledge sources and networks, and has increased the depth and variety of scientific competences of the local mix, thus facilitating more robust information filtering networks (Gertler and Levitte, 2005; Graf

and Krüger, 2011; Eisingerich et al, 2012).

7.2.2 PREO networks with commercial actors (Bio-firms and TNCs)

PREOs proactively promote the transmission and dissemination of information by adhering to "the norms of the open information disclosure characteristic of public science" (Smith and Powell, 2004: 8) through lecturing, publications, academic and industrial placements, and conference presentations (McMillan et al., 2000).

Yet, the manner in which a research programme's findings are ultimately codified, i.e. through a publication or a license development, reflects the commercial orientation of a programme's academics. Traditional research-orientated academic scientists focus on producing journal publications and/or conference presentations, while commercially minded entrepreneurial academic scientists seek to engender formal commercial developments, i.e. a patent development or start-up bio-firm development, where commercially viable Intellectual Property (IP) is generated (Casper and Murray, 2005; Malecki, 1997).

Additional formal commercial alliances which form between PREOs and commercial actors, i.e. bio-firms and TNCs, include relatively limited collaborative R&D agreements, research agreements (with no development elements), and relatively minor research grants. For the academics, these relations are motivated by strategic and economisation motives of accessing the financial resources and technological capabilities of the commercial actors, so as to commercialise research, while they also allow academics to gain insight into emerging industrial trends, needs and requirements (Casper and Murray, 2005; Smith and Powell, 2004; Giesecke, 2000; Lundberg and Andresen, 2012).

Due to the decades of public under-investment in the infrastructures, resources and skills of the various Irish PREOs (as detailed above), their research capabilities and activities were heavily restricted, which limited the level of information PREO researchers could produce and disseminate. PREO respondents stated that where pre-initiative codified outputs emerged, they overwhelmingly took the form of academic publications for a variety of interlinked reasons.

Academic publications were the central elements in the pre-initiative promotion procedures of the PREOs, i.e. licensing developments were not included in such

procedures, meaning few researchers proactively sought their development. A RI-based interview respondent noted "a lot of researchers did work that just sat on a shelf...all they had to do is go a bit further to commercialise something, but there was no motivation" (RI respondent 3, interview).

The commercial orientation of all pre-initiative PREO actors, "from the administration right through to the researchers...[was very poor, as] historically, Universities weren't bothered in commercial collaborations" (RI respondent 3, interview). This scenario developed due to the virtual absence of commercial elements in the limited public actor PREO development initiatives, i.e. pre-initiative public funding was predominately block funding in nature and was allocated without any specific or explicit commercialisation requirements.

As such, no commercialisation pressure or motivation existed or developed among PREO actors. This resulted in the development of an entrenched approach towards commercialisation among academics and administrators. A university respondent commented

> "…academic involvement with industry was seen as not being desirable, the notion [among academics] was [that] the researchers were pure and should avoid industry. There was an element of 'this person is from industry, they don't know anything about science, [that] they are just purely money driven`" (University respondent 7, interview).

A university respondent commented that "one administrator [in the mid 1990s] said to me `Don't bother [collaborating with commercial actors], you'll never get your money off them`" (RI respondent 5, interview). Another university respondent commented that "the main issue used be with the university's administration....very often they scored own goals by making the firms [i.e. commercial actors] go away...[because of a] lack of interest, or unreasonable views" (University respondent 6, interview).

In combination with the PREOs' limited research capabilities, these issues strongly inhibited formal alliance developments with the bio-sector's commercial actors, i.e. few patent developments or start-up bio-firms emerged or originated from the pre-initiative PREOs. Yet, such developments were further restricted by the limited financial resources and technological capabilities of the sector's bio-firms, TNCs and investor actors, as detailed in the following section. This meant that PREO actors had limited opportunities and capabilities to gain insight into industrial trends in the indigenous bio-

sector, its needs and/or requirements.

Where downstream commercial alliances developed, they primarily formed with non-Irish downstream actors as PREO researchers sought to by-pass the indigenous bio-sector's shortcomings. These collaborations were overwhelmingly formal in nature due to the limitations of the PREOs, i.e. they predominantly took the form of defined research investigations into the specific behavioural aspects of products/processes. In some cases the non-Irish collaborator would conduct parallel in-house investigations and use the PREO-based research simply to compare and validate their findings. Several academics commented that such alliances typically arose from non-Irish actors establishing contacts through accessing journal publications, conference presentations, and/or through contacts with former graduates or colleagues who had taken up employment in the non-Irish sectors.

The various issues and limitations of the PREOs also meant that researchers were generally unable and/or unwilling to participate in the various European Union (EU) programmes which sought to facilitate EU-wide PREO alliances with commercial actors (Appendix C), in particular as these programmes required PREO applicants to have pre-existing collaborations with industry-based actors. Additionally, the bureaucracy levels of these programmes were excessively prohibitive, while their prescribed timescales were generally unsuitable for academic researchers.

The capabilities and resources of Irish PREOs have advanced due to the on-going Government development initiatives. These initiatives have facilitated increased information transmission and dissemination through 'traditional' avenues, e.g. journal publications, yet they have also facilitated crucial patent developments and engendered more advanced formal alliances between PREOs and commercial actors, particularly research and/or development agreements, and joint ventures.

The main factor driving these developments is the defined commercial emphasis of the on-going initiatives. This has strongly impacted on and changed the commercial orientation of the PREOs and their administrators and academics. A university commercialisation respondent stated that “there has been a huge change in their approach [i.e. the commercialisation approach of the public agencies], but what has also been crucial has been the overall money that's now available” through the various

initiatives (University commercialisation respondent 1, interview).

Agency actors are increasingly proactive in facilitating commercialisation developments among PREOs, while a key development, highlighted by several interview respondents, has been the augmentation of the types of funding available to PREO actors. One university respondent, with extensive industry experience, commented that the switch from block grants towards competitive funding sources has contributed towards the increased commercial orientation among PREOs as "the academics have to compete for funding, before they really didn't. This means they are now also beginning to see commercial rewards as an alternative source of funding" (University respondent 1, interview).

The post-initiative bio-firm developments have also augmented the entrepreneurial character and environment of the indigenous bio-sector. Their establishment demonstrates to commercially minded PREO actors that successful commercial developments are possible through the current support structures, potentially "open[ing] up an entrepreneurial spirit that is clearly missing [in PREOs]" (Investment respondent 1, interview).

Additionally, the attraction of non-Irish researchers through the TFF has been crucial in augmenting the commercial orientation of Irish academics and in engendering a more pronounced entrepreneurial mind frame due to their more pronounced commercial nature. As detailed above, these academics have added to the local 'buzz', and have created a more fertile innovation dynamic through increasing idea diversity within Ireland's knowledge base. A TTO respondent commented:

> "By attracting these [non-Irish] researchers, you've now got a huge range of background and approaches. So I see it as success breeding success...if I see a guy arriving at work driving a fancy car that he bought as he successfully commercialised something, I'll say 'I can do that too.' So this is driving things along...it's the returns for licensing that will drive the developments, the monetary rewards..." (TTO respondent 5, interview).

This comment was echoed by a development agency respondent:

> "We are beginning to see a kind of competition; 'Well that guy is earning so much from a patent that he has licensed to BASF or to Pfizer, and I'd like some of that too.' This kind of competition...we are seeing an increase in patenting, which is a primary indicator of people moving towards commercialisation. It's still early days, but certainly much more promising" (Development agency respondent 2, interview).

A VC respondent commented that these developments have engendered a noticeable

change in the commercial orientation of academics since the late 1990s:

> "it is less typical to find...[a new academic] who has gone from undergraduate, to post-graduate, to post-doc[torate], and into to full time academic work without experiencing anything else. Most of the new lecturers...I've noticed that I meet more with a business edge to them, more than I would have, definitely" (VC respondent 2, interview).

Supporting and complementing these efforts to engender a more pronounced commercial mind set amongst Irish PREO actors, in relation to the commercial orientation of their research and the formation of downstream developments, has been the development of infrastructures and resource supports that seek to both encourage and facilitate entrepreneurial developments. These include:

- the augmentation of PREO promotion procedures to include licensing developments. This has resulted in the "publish or be damned [attitude] being replaced by [a] publish, and you loose IP mindframe" (PREO respondent 4, interview),
- the addition of defined commercialisation elements to the employment contracts of post-initiative academics,
- the upgrading and expansion of the capabilities, resources and activities of the different Technology Transfer and Industrial Liaison Offices (TTOs and ILOs),
- the introduction of intermediary actors to facilitate PREO/downstream alliances, such as Enterprise Ireland's (EI) bio-incubators, and SFI's Centres for Science, Engineering & Technology, and
- the introduction of dedicated commercial supports, including VCs and the various commercialisation-orientated funds of EI, to drive commercial developments from PREOs.

However, while these developments have resulted in more advanced commercial alliances and developments between PREO actors and downstream actors, e.g. the emergence of the post-initiative bio-firms, and have fed into and further enhanced the commercial orientation of PREOs, the overall level of "commercialisation know-how amongst Irish academics is not an integral/intrinsic part their of their knowledge set" (Forfás, 2004: 103). This comment was echoed by several interview respondents; an investment respondent commented that "the business side [of PREOs] hasn't grown as fast as the science aspect...technically they are up there, but commercial management in

Universities is still very poor" (Investment respondent 1, interview). A university-based respondent commented that "...what is important is having people who can interact with companies and who have a very clear commercial focus...having the people who can go out then and sell the concept, sell the products. They simply aren't there" (University respondent 4, interview).

Additionally, commercial developments are restricted by the limited number of indigenous downstream outlets for PREO research. One academic respondent commented that "[government] funding has only focused on idea generation...while the universities have developed, there really isn't an industry in Ireland" (Academic respondent 6, interview).

Pre-initiative bio-firms remain engaged in activities that limit possible alliances, while the post-initiative bio-firms are in the relatively early stages of their development and have yet to reach a point where further alliances can form (these issues are discussed further in the following section). Additionally, many academics, particularly those engaged in diagnostic-based activities, state that severe difficulties remain in their ability to form alliances with Irish-based TNC operations. Despite the development of more research-orientated activities in their operations, the TNC operations remain essentially branch plant in nature due to their on-going limited autonomy:

> "TNCs in Ireland still have no real research activities, they have no research ethos that I can link into…their research programmes are basically all laid out for them, with specified goals and targets. None of their [research] programmes developed from their own activities, they are just imported from the research centres in the US, or Switzerland" (PREO respondent 8, interview).

Even with the increased level of PREO and post-initiative bio-firm activities, "there remains limited appeal for TNCs in Irish research activities...we're trying to develop links, but there isn't much here at the moment that we'd want to, or can link into" (TNC respondent 1, interview).

The improved international image of the PREOs engendered through the PRTLI and TFF (as detailed above) has facilitated an increased though still limited number of alliances with non-Irish downstream actors. These alliances remain predominantly formal in nature, i.e. defined resource and knowledge transactions, and most commonly take the form of:

- commercial research grants, i.e. commercial actor sponsored post-graduate research projects, particularly research masters degrees due to their short time frames. A PREO correspondent commented that the "simple research based grants can be quick...[they are usually] funded for 3 years, though we do get involved in smaller programmes that can take around one to one and a half years to complete" (PREO respondent 3, interview). This respondent also stated that the commercial actors are effectively getting high quality research for very small sums of money through such grants;
- research (no development) agreements with commercial actors. These agreements involve investigations of the behavioural aspects of firm-developed products/processes, and take the form of strictly defined collaborative agreements which end once the programme reaches its testing phase. After this phase ends, the commercial actor assumes control of the succeeding development stages;
- 'joint venture' developments between academics and commercial actors. Unlike joint ventures found in the international bio-sector, such ventures have strictly defined parameters, where the development aspect of these arrangements occur solely in the non-Irish-based product/process development facilities of the partner TNC, and;
- licensing agreements between academics and non-indigenous bio-firm and TNC operations. So far, such developments have been extremely limited in number.

7.2.3 Upstream bio-firm networks with PREOs

Bio-firm/PREO alliances represent the first downstream stage of the biotechnology innovation process, i.e. research enters the product development process. At this point of the bio-sector's innovation process, PREOs represent the network structure's dominant actor type for a variety of reasons. Internationally, bio-firms are predominantly founded by entrepreneurial academics, and locate in close proximity to their 'parent' PREO. Close proximity and social inclusiveness with PREOs determines a bio-firm's research capabilities by influencing the formation and maintenance of close social relationships which facilitate access to 'filtered' tacit and codified commercially viable knowledge. These features are increasingly important due to the niche orientated nature of bio-firms internationally. Additionally, formal business competence exchanges facilitate transfers of organisational routines during the initial stages of a bio-firm's development, while bio-firms also seek to access skilled human capital from PREOs (Owen-Smith and Powell, 2008; Powell and Brantley, 1992; Romanelli and Feldman,

2007; Malecki, 1997; Graf and Krüger, 2011; Eisingerich et al, 2012).

Pre-initiative upstream networks between Irish bio-firms and PREOs were very limited for a variety of reasons, including:

- the poor commercial orientation and support structures of the PREOs, as detailed above;
- the presence of employment regulation rigidities among the PREOs which prevented personnel exchanges between bio-firms and PREO actors, and;
- the conservative nature of the pre-initiative bio-firms, i.e. their diagnostic activity focus.

As such, Irish PREOs did not form the core origin points of the overwhelming majority of the pre-initiative bio-firms, as these bio-firms by-passed the limited availability of commercially viable indigenous research through forming licensing agreements with non-Irish PREOs. A pre-initiative bio-firm respondent commented:

> "…we're a diagnostic firm with no Irish [PREO] links...If we were based in the US then we'd have collaborated more with university researchers…when the company started, there was very little here [in Ireland] we were interested in linking into. In fact, there was very little we could link into" (Bio-firm respondent 5, interview).

Where collaborations formed between the pre-initiative bio-firms and indigenous PREOs, restrictive contract-based research collaborations developed. These were typically short-term bio-firm sponsored postgraduate research projects with very narrowly defined targets, i.e. minimal informal and/or formal resource and knowledge transactions formed, which inhibited spillover developments.

Despite the on-going post-initiative sectoral developments, these relationship characteristics still define the pre-initiative bio-firms, as they have essentially been by-passed by the various initiatives. This issue is detailed further in the following chapter.

In relation to the post-initiative bio-firm developments, over 30 post-initiative 'Genentech template' bio-firms having been created over the last ten years from research originating from the new RIs. These post-initiative bio-firms mimic the organisational and locational trends of bio-firms in the international bio-sector by locating in close proximity to their 'parent' PREOs. These developments have seeded important strengths in the bio-sector.

Due to the nature of their origin, and their ability to access and exploit the increasing PREO-based activities and the more advanced indigenous and international skills and knowledge sets which have been retained and/or emerged in the country's PREOs, more advanced informal tacit/embodied knowledge exchanges have developed with PREO actors, relative to the pre-initiative exchanges. This means that key upstream relationships found in international hub bio-sectors have developed, i.e. Irish PREOs are the key actors in the upstream end of the post-initiative bio-firms' innovation processes (Enterprise Ireland, 2007; Krafft et al., 2011).

However, the overall level of alliances between the post-initiative bio-firms and Irish PREOs remain limited due to their relative age and size, yet they are expected to advance as the bio-sector's development progresses. The on-going limitations in the commercialisation experience and orientation of PREO actors, as detailed above, means that limited exchanges of resources continue to occur. Additionally, on-going employment regulation rigidities continue to restrict personnel exchanges among PREOs and bio-firms, particularly by preventing bio-firm founders from maintaining academic appointments following a bio-firm's formation.

7.2.4 Downstream Bio-firm networks with commercial actors

The downstream network arrangements of the Irish bio-sector's pre-initiative bio-firms were strongly shaped by the sectoral actors' weaknesses at either end of the bio-sector's innovation process. The restricted innovative activities of the PREOs meant pre-initiative bio-firms adopted conservative business models in areas where little research activity occurred, and/or in which collaboration was essentially superfluous to requirements, e.g. diagnostics- or specialist supply-based activities.

Additionally, their conservative nature developed in response to the general absence of the 'traditional' commercial supports, infrastructure and services found in hub bio-sectors, particularly dedicated VCs. A very limited number of pre-initiative bio-firms received VC investments, and only when they approached the later stage of their development, i.e. when prospective investment returns were more clearly defined. A bio-firm respondent in one such bio-firm commented that this approach "was wrong, completely against the supposed purpose of a VC" (Bio-firm respondent 7, interview).

Due to these issues, bio-firm respondents commented that they actively sought non-Irish

VC funding. However, they had very limited success in establishing such alliances as "...there really wasn't any track record of success in Irish investment in life sciences, potential investors were quite nervous about getting into the [Irish] sector" (University respondent 3, interview).

Furthermore, the possible downstream alliances bio-firms could develop were limited due to the manufacturing-orientated nature of the TNC branch plants, while inter-firm networks were heavily restricted by the lack of overlap between their activities due to their conservative niche nature.

Where pre-initiative bio-firms established downstream alliances, they primarily developed with non-Irish actors, i.e. the bio-firms sought to access skill-sets and resources that were unavailable indigenously. However, a very limited number of indigenous downstream relationships did develop, predominantly through pre-existing contacts firm-based actors had previously established while working in other areas of the bio-sector.

Despite such origins, these were restricted formal alliances due both to the nature of their activities, and also due to the sectoral context in which they emerged. Additionally, a very limited number of inter-firm equity alliances (buy-outs) occurred when relatively larger diagnostic bio-firms acquired the IP of smaller bio-firms so as to expand their product range. No downstream joint-research, R&D, development alliances developed, while manufacturing and marketing alliances were virtually non existent.

In the post-initiative bio-sector, formal post-initiative downstream networks remain predominately with non-Irish actors, though this is slowly changing as sectoral activities gradually develop.

Inter-actor downstream networks in the post-initiative bio-sector remain limited for a variety of reasons. The continuing limited nature of the bio-sector's actors, in terms of numbers, variety and activity restricts their development, e.g. bio-firm activities still do not overlap to an extent that facilitates inter-firm collaboration(s), while the pre-initiative bio-firms remain small and conservative in nature. Despite the post-initiative bio-firms having a defined commercial orientation due to the manner of their origin, commercial linkages in the bio-sector have yet to noticeably advance due to the time lag

between their foundation, i.e. most of the post-initiative bio-firms are around 5 years old, and when they are expected to produce commercial products, i.e. the majority of these bio-firms have yet to reach the point where they can enter into networks with other commercial actors.

Commercial developments are also being restricted by the presence of various issues relating to investor actor coverage and involvement in the Irish bio-sector. The bio-sector's investor coverage is essentially limited to the post-initiative public VCs, i.e. there is too limited a range of investor actor types, such as seed investors, in the indigenous sector. This limits the type of commercial developments that can occur in the indigenous sector, as:

> "not everything [i.e. commercial development] will suit a VC firm. Because there really are no other kinds of investors, projects with real promise will be overlooked...that means everyone is trying to fight for the same funds. That won't work, you are too limited with what you can go for, and in what they will look out for" (University respondent 1, interview).

However, many interview respondents commented that the level of indigenous VC funding, as a whole, is "not enough to develop a drug in Ireland" (Bio-firm respondent 5, interview), and is barely sufficient to support the first stages of a clinical trials research processes. Several respondents, including a VC actor, noted that even if an indigenous research programme reached the second stage of clinical trials, none of the indigenous VC firms have sufficient funding levels to completely finance such trials.

Additionally, VC coverage in Ireland is overwhelmingly concentrated in the GDA. This is a significant sectoral issue, as internationally VC funding is spatially concentrated due to its reliance on informal networks. VCs characteristically only 'expand' their coverage to non-local areas when a bio-sector matures and delivers visible commercial promise. The limited commercial activity in the Irish bio-sector means that the GDA focus will continue for some time, and will paradoxically undermine non-GDA commercial developments as GDA-based developments advance.

Several interview respondents stated that they had sought funding from non-Irish investors in order to by-pass these issues. One bio-firm respondent commented that he had "spoken to a number of VCs outside Ireland...[we] met with a VC representative in the States who represented about 20 different VC companies in the New York area" (Bio-firm respondent 6, interview). However, this respondent noted that this strategy is

problematic as the Irish bio-sector remains perceived as having a "...really poor [track] record. The investors still feel too unsure about the possibilities of successfully developing a company here" (Bio-firm respondent 8, interview).

In relation to downstream alliances between Irish sectoral actors and TNCs, they continue to be limited by the on-going manufacturing-orientated nature of many of the TNC operations in Ireland. This situation remains despite the increased number of research-orientated TNC operations which have been set up in the country through the on-going efforts of the IDA Ireland, and the development of key intermediary actors between TNCs and PREOs, i.e. the Centres for Science, Engineering & Technology.

In part, this is due to the new TNC operations being essentially R&D branch plants that have little autonomy over the research programmes they conduct. Their nature undermines the development of alliances with sectoral actors. Additionally, their research activities are characterised as being close to the end of the applied research phase/at the beginning of the product development process, which means they are engaged in activities that are too advanced for linkages with PREO actors to develop.

However, due to their more pronounced research focus, a limited number of TNCs have begun to explore opportunities of linking up with PREO-based research programmes. Yet, as one TNC respondent stated, "a lot of work and restructuring has to occur [in the Irish PREOs] before it begins to happen" (TNC respondent 2, interview).

This echoes comments made by another TNC respondent, i.e. that there is still too little sectoral activity 'across the board' for TNCs to develop significant alliances with sectoral actors. Essentially, the limited track record of the indigenous bio-sector in developing biotechnology-derived products/processes, and the absence of a sectoral 'star' bio-firm development, means that TNCs from hub bio-sectors remain unconvinced about the commercial potential of the bio-sector.

Additionally, the costs of establishing and maintaining long distance alliances with such an unproven bio-sector are perceived as being prohibitively high. One investment actor noted that TNCs will "...only start getting interested [in indigenous] firms when they get near the clinical trial stage, but...many products can't be brought up to the point where [TNCs]...would get interested because the firms don't have the resources or finance to

do so" (Investment respondent 1, interview).

In a proactive response to the limited scope of the bio-sector, a limited number of post-initiative bio-firms have augmented their 'traditional' activities. Several bio-firms have provided consultancy services to commercial actors from related indigenous sectors that they have either identified and/or been approached by, and which are interested in adopting biotechnology-related processes and/or entering the bio-sector. Such services seek to inform these actors about the unique demands, activities and opportunities available through biotechnology, and which are present in the indigenous bio-sector. Additionally, several bio-firms have begun hosting training and lecturing programmes on biotechnology in order to address particular knowledge gaps they have identified in certain areas of the bio-sector and related sectors.

These supplementary activities constitute a form of indirect network development in the bio-sector. A bio-firm respondent noted "...there have been some changes in the types of contracts we have taken, and with the types of clients or customers we've had" (Bio-firm respondent 1, interview) as a direct result of these activities. These developments have engendered limited spillover developments, through combining different sources of knowledge and resources.

7.2.5 Sectoral support actor networks

The main international bio-sectors develop extensive regional-specific public and private sectoral support structures, which include private investment actors and specialist supply firms. These support actors facilitate and drive sectoral developments through engendering close alliances with the main actors in the sectoral value chains.

As stated above, the pre-initiative bio-sector's support structures were extremely limited due to its limited innovative activities. This, paradoxically, fed into the limited nature of the sectoral support structures:

- private VC actor involvement in the bio-sector (as detailed above) was limited by, and fed into the conservative nature and limited research activities of the bio-firms,
- indigenous supply firm activities were restricted by, and fed into this limited activity level, and
- no sectoral trade associations or sub-national biotechnology centres existed.

Due to these support limitations, sectoral actors proactively sought alliances with non-Irish supply firms. Yet, paradoxically, the limited level of sectoral activities meant that the main customer markets of the pre-initiative supply firms were in other EU countries, particularly the UK. These issues inhibited crucial knowledge, resource and skill transfers, which undermined sectoral innovative developments.

Significant issues remain in the range of professional supports that indigenous actors can presently access in the bio-sector. The on-going post-initiative sectoral developments have largely been facilitated and driven by the introduction of dedicated public sectoral supports, in particular the dedicated public VCs and the advanced PREO commercialisation support, e.g. the bio-incubators introduced by EI. Yet, very limited private specialist supports have formed in response to these developments to address the more advanced needs of the bio-sector.

Additionally, the public supports are conservative in nature due to their public nature, their relative age, and also as the Irish bio-sector's ultimate commercial potential has yet to be established. Furthermore, they overwhelmingly focus on the post-initiative bio-firms.

Overall, the limited numbers of suppliers means that sectoral actors continue to develop extensive linkages with non-Irish supply firms out of necessity. As such, the accumulation of specialist cores of knowledge in the bio-sector remain restricted, i.e. the support services are not specialised on the particular needs of the bio-sector's actors, meaning Irish actors have to rely on relatively more generic goods and services from non-Irish sources. This further limits inter-actor interaction and spillovers in the indigenous bio-sector.

Furthermore, the number of indigenous private supply firms remains limited due to the continuing limitations in the activities of the indigenous bio-firms. One supply firm respondent stated that Ireland is "...still a fairly small market, relatively speaking. Overall, there is always room for more" (Supply firm respondent 2, interview). Supply firm respondents commented that their main customer markets remain in other EU countries, which also means that bio-firm and PREO actors continue to have extensive supply networks with supply firms in other EU countries.

In relation to sectoral trade associations, several associations have emerged since the late 1990s, e.g. the Irish BioIndustry Association. These developments have facilitated significant flows of tacit knowledge among sectoral actors. However, their overall impact has been limited by the overall state of the bio-sector's activities. Additionally, several respondents identified the lack of coordination among the different association actors as undermining collaborative developments. Furthermore, no clear regional focus, co-ordination or interaction exists among them, which is limiting and fragmenting important inter-actor business and competitive intelligence exchanges.

Overall, these support actor issues mean that crucial knowledge, resource and skill transfers remain limited, which continue to restrict sectoral innovative developments.

7.3 DISCUSSION ON THE IRISH BIO-SECTOR'S NETWORK STRUCTURE

There are two broad identifiable forms in how the bio-sector's innovation process is replicated internationally, i.e. hub and non-hub bio-sectors.

The network structures and innovation processes of global hub bio-sectors act like a collective entrepreneur, where actors form dense concentrations, i.e. critical masses, of regional specific skills, resources, information and networks, which facilitate the rapid transfer and diffusion of information/knowledge and resources, and engender sector-wide innovative developments and self-supporting and generating regional agglomerations (Anderson et al., 2004).

Hub bio-sectors are defined by the two inter-related downstream sectoral network forms, i.e. vertical and horizontal downstream networks, extensive region-specific public and private support structures, including public and private investment actors and specialist supply firms, a sectoral 'brand' that advances actor networks and sectoral support structures through facilitating extensive external alliances, and significant labour pool diversity, which facilitates significant knowledge spillovers and drives sectoral network density (Anderson et al., 2004; Feldman, 2001; Malecki, 1997; Delerue and Lejeune, 2011).

Outside of the global hubs, bio-sectors are essentially little more than combinations of co-locating actors, principally bio-firms and PREOs, grounded in regional ambitions to become significant bio-sectors. Their network structures are poorly developed, characterised by limited innovation levels caused by region specific limitations in actor

numbers, resources, skills and specialist suppliers. To compensate, a common strategy for non-hub actors is the development of distant collaborative network strategies with more knowledge and resource rich bio-sectors, so as to access resources, skills, and competences missing in their indigenous bio-sectors. Yet, such strategies face significant issues as the poor innovative image/reputation of a bio-sector will dissuade non-local actors from entering into such alliances, while non-hub actors face intense competition for these resources from more dynamic bio-sectors. Where such strategies fail to materialise, less endowed hub bio-sectors experience cumulative disadvantages, and fall further behind relative to the hub bio-sectors (Powell et al., 2002; Gertler and Levitte, 2005; Malecki, 1997; Casper, 2007; Morris, 2011).

The pre-initiative bio-sector's network structure was compromised by a general absence of sectoral actors and activity. The bio-sector's innovation process was heavily compromised by the poor development of the different PREO actors, due to decades of public underinvestment. Their restricted research activities and characters were reflected in the limited and conservative nature of the bio-sector's bio-firms, which were compounded by the general absence of sectoral supports, particularly VCs. Commercial activities were also compromised by the relative absence, or lack of participation of key downstream actors in the bio-sector, in particular TNCs.

Overall, the pre-initiative bio-sector's network structure can be characterised as having been non-hub in nature, i.e. groupings of conservatively structured actors which engendered limited spillovers due to their poor networking arrangements with indigenous actors, and whose main networks were with non-Irish actors as they sought to by-pass the chronic shortcomings of the indigenous bio-sector. The lack of sectoral innovative activity meant no sectoral branding occurred, which undermined these alternative proximity strategies. In combination, these various issues undermined the bio-sector's development trajectory.

Due to the PREO centric focus of the on-going public development initiatives, more significant network activities have formed in the upstream end of the bio-sector, yet a critical mass of sectoral actors, activities and networks has not formed.

PREO-based networks resemble networking patterns found in the hub bio-sectors, due to the advanced research activities of the post-initiative RIs and their close proximity to

their 'parent' university facilitating significant spillover developments. Additionally, transfers of this increased research activity into commercial concerns, i.e. the post-initiative 'Genentech Template' bio-firms, has occurred through the introduction of Government-sponsored commercialisation supports, i.e. PREO-based innovation centres (incubators) and dedicated VCs. As such, more extensive intra-PREO and PREO/bio-firm networks have developed, facilitating key transfers of filtered tacit and codified knowledge and resources.

Yet, significant systemic weaknesses remain in the bio-sector's network structure. The ability of pre-initiative bio-firms to form collaborative networks remains constricted by the presence of an established innovation paradox. Additionally, a time lag has developed between the emergence of the post-initiative bio-firms and their ability to enter significant downstream collaborative alliances. These issues are amplified by the on-going limited level of supply firm developments, and the continuing minimal involvement of Irish-based TNC operations in the bio-sector.

In combination, these issues mean that a sectoral 'brand' has not emerged, which continues to limit the bio-sector's ability to attract in key non-local actors and skills (these issues are discussed further in the following chapter). Overall, the Irish bio-sector's network structure remains non-hub in nature.

A key issue undermining network developments in the bio-sector is the established, long-term absence of network elements in previous and on-going Government industrial policies, despite successive Government sponsored publications since the 1980s having called for their introduction (Forfás, 2004; Edquist and Hommen, 2008).

This scenario also remains despite networks being noted by Government agencies as being key elements in the bio-sector's development. A government agency respondent commented that the right “leadership needs to be in place. While the interest is there [among government actors], they haven't figured out how to do it” (Government agency respondent 2, interview).

Government agencies are seeking to develop inter-actor collaborations, yet not as part of a defined collaborative networking programme. Agencies are using funding to essentially force actors to collaborate, predominantly to facilitate more optimal and

efficient uses of personnel and resources. Respondents with experience of EU-funding-induced collaborative initiatives, upon which these efforts are based, commented that such collaborations typically end once a project ends due to their contractual nature, i.e. the collaborations are not trust-based networks. Where trust is absent, actors will sacrifice potential gains derived through co-operation by pursuing self-interests due to the perception of risk (Forfás, 2004: Government of Ireland, 2007).

This issue feeds into the absence of regional development elements in the on-going initiatives, as detailed in chapter 6. As with actor endowments, regional differences exist in how the Irish bio-sector's network structure has developed. Three main concentrations can be identified in the indigenous bio-sector, i.e. the Greater Dublin Area (the GDA), and the Cork City and Galway City regions. The GDA has the largest and most developed network structure in the bio-sector due to its larger actor and activity concentration. Essentially, the GDA's more complex endowments of infrastructures, skills and resources have facilitated more advanced spillover developments, and has advanced at a greater rate relative to the Cork and Galway City regions, while also continuing to draw away skills and resources from these regions (DETE, 2003: InterTradeIreland, 2003; Chen at al., 2011).

Overall, the Irish bio-sector's network structure is poorly developed due to significant on-going sectoral actor weaknesses, and the absence of a suitable policy environment which addresses the interactive, inter-linked and inter-dependent elements which characterise and typify the international bio-sector's innovation process.

CHAPTER 8:
POLICY PROPOSALS FOR THE DEVELOPMENT OF THE INDIGENOUS BIOTECHNOLOGY SECTOR

8.1 INTRODUCTION

This chapter presents a set of policy recommendations relating to the future development of the indigenous biotechnology sector (bio-sector). The chapter is divided into three sections. The first section presents a general review of various strengths which have developed in the indigenous bio-sector, on which future sectoral development initiatives may build, as well as the various weaknesses which may/will undermine on-going and future sectoral development efforts. These areas are analysed in relation to the Irish bio-sector's value chain, its actors and their activities, and are also analysed in the context of observable development trends in the international bio-sector. The second section proposes a comprehensive policy framework which seeks to coordinate the indigenous bio-sector's development in a systems-based manner so as to engender the conditions which will optimise entrepreneurial and innovative activities across the entire bio-sector. This framework is derived from the entrepreneurial and innovative functional resource themes presented in chapter 3. The final section concludes the chapter.

8.2 A REVIEW OF THE INDIGENOUS BIO-SECTOR'S GENERAL STRENGTHS AND WEAKNESSES

8.2.1 General sectoral strengths

The indigenous bio-sector has undergone significant and substantial developments through the on-going Government initiatives that have been introduced since the late 1990s. Significant sectoral strengths have been seeded, particularly as a result of the Programme for Research in Third Level Institutions (PRTLI) and Science Foundation Ireland's (SFI) Technology Foresight Fund (TFF).

Their size and long-term nature have seeded important strengths in the PREOs, specifically through facilitating the development of actor and institutional density through the formation of a world class science base. This is creating “strong foundations that the industry can now be built on” (Investment respondent 1, interview).

The PRTLI has facilitated key infrastructural, resource, and skills developments that have resulted in significant advances to the capabilities and activities of the PREOs and their actors. A crucial PRTLI-related sectoral development has been the introduction of the commercially orientated post-initiative research institutes (RIs). Their defined

collaborative orientation has been important in engendering key spillover developments within the PREOs, as well as feeding into and driving downstream sectoral developments (discussed further below).

Parallel to the PRTLI, the TFF has allowed the PREOs to retain skilled indigenous researchers, and also to attract high skilled internationally renowned 'star' researchers into Ireland. The TFF has also created a limited 'brand' effect which has attracted in non-Irish researchers, facilitating crucial spillover developments and skill transfers, and advertised the PREO-based developments and their improved and increased skills, activities and facilities to the international research community and to the wider international bio-sector in general.

The increased PREO research activity these developments have engendered has been complemented by the introduction of more substantial commercialisation support structures and resources in the PREOs. The capabilities and resources of the PREO's Technology Transfer (TTO) and Industrial Liaison (ILO) offices have been upgraded and expanded, while important new intermediary actors between PREOs and downstream actors have been developed, e.g. the incubators introduced by Enterprise Ireland (EI). These supports have been complemented by the introduction of different commercialisation-orientated funds by EI, which particularly focus on optimising commercial developments originating from the new RIs.

Supporting and complementing these supports have been proactive efforts to engender a commercial mind set amongst PREO actors, in relation to the commercial orientation of their research and the formation of downstream commercial developments. These efforts are being driven through the augmentation of the PREO promotion procedures to include patenting and licensing activities, and the addition of defined commercialisation elements to the employment contracts of 'new' post-initiative academics. Additionally, the TFF has contributed to the engenderment of a more pronounced entrepreneurial mind-frame through allowing PREOs to draw in industry-based researchers when sourcing potential employees.

These PREO-based developments have been complemented by public actor efforts to engender an environment in the wider bio-sector that supports commercial downstream developments. These efforts have created significant strengths, relative to the pre-

initiative bio-sector, and include:

- the crucial emergence of post-initiative bio-firm developments, and;
- the introduction of dedicated VCs.

The composition of the downstream end of the bio-sector's value chain has grown in complexity through post-initiative 'Genentech Template' bio-firm developments. They have emerged due to the introduction of dedicated commercial supports, particularly the introduction of dedicated VCs, which seek to exploit the increased levels of PREO-based research. These developments have augmented the bio-sector's entrepreneurial character and have also advanced its international reputation.

The emergence of the post-initiative bio-firms has created limited, though important positive sectoral feedback events. Through the nature of their origin, i.e. the exploitation of indigenous PREO-derived IP, they have demonstrated the bio-sector's latent commercial potential to commercially minded sectoral actors, in particular academics, and have advertised the depth and quality of the bio-sector's commercialisation supports, thus encouraging increased commercial developments from within the PREOs.

Additionally, the introduction of dedicated VCs is a crucial development in optimising the bio-sector's development trajectory, specifically through facilitating the post-initiative bio-firm developments, and also through advertising the more complex commercialisation supports which exist in the bio-sector to commercially minded researchers, and to international actors.

8.2.2 General sectoral weaknesses

Despite the impacts of the on-going initiatives, a significant range of interlinked sectoral issues/weaknesses exist that are obstructing and undermining the optimal development trajectory of the bio-sector.

8.2.2.1 PREO-based weaknesses

The majority of the sectoral developments engendered by the on-going initiatives have been heavily concentrated in and around the country’s PREOs. However, the continuing legacy of decades of underinvestment in the country's PREOs prior to the late 1990s and the resultant limitations in the availability of equipment and skills means that significant weaknesses remain in the structures and activities of the PREOs. These include:

- the relative absence of funding for basic research programmes;
- key skills weaknesses;
- on-going structural weaknesses;
- the on-going weak commercial orientation of administrators, academics and students;
- on-going weaknesses among sectoral commercial support and intermediary actors, and;
- the continuing limited commercial 'marketing' by PREOs.

8.2.2.1.1 Basic research funding weaknesses

The on-going funding programmes have focused overwhelmingly on applied research. This focus can be explained by the distinct commercialisation drive/impetus attached to the initiatives, the importance of a strong science base for sectoral developments, and the finite resources available to the Government. Indeed, several respondents acknowledge that the funding bodies wish to maximise their returns for the money invested, as "you can spend years on a basic research topic, and it can happen that soon it becomes outmoded, or someone does something that makes that research irrelevant...The pace is too fast for purely speculative research" (PREO respondent 2, interview).

However, respondents commented that this applied research focus is too limited and short-sighted, and will become a significant long-term weakness, as "you need basic research to feed into applied activities...they are both as important as the other" (PREO respondent 1, interview). This comment reflects statements expressed in several government publications. The Science, Technology and Innovation Advisory Council report (1995) commented that a balance had to be reached between applied and basic research, while the Department of Trade, Enterprise and Employment (2006) noted that "...attempts to build a system of applied research without a base of excellence in the underpinning sciences [i.e. basic research] are not sustainable" (Department of Trade, Enterprise and Employment, 2006: 22).

Additionally, despite several definitions of basic and applied research activities being presented in Government publications, through the Government agency respondent interviews, it is apparent that a certain level of confusion exists as to the distinction between both forms of research, e.g. a government agency respondent commented

"…basic research is commercial [i.e. applied] research" (Government agency respondent 2, interview).

8.2.2.1.2 Key skills weaknesses

Three main PREO-based skills weaknesses presently exist, as identified by sectoral respondents.

Firstly, the numbers of new students entering third level science courses are declining due to the low take up of science subjects at secondary level education. This has the potential to develop into a major competitive disadvantage for Ireland, by restricting the skills supply to the indigenous bio-sector. It must be noted that this issue is outside of the remit of this project (Forfás, 2003, 2007; van Egeraat and O'Byrne, 2010).

Secondly, prior to the introduction of the on-going initiatives, a graduate 'brain drain' from the PREOs existed, i.e. many graduates left Ireland due to the limited sectoral employment opportunities. While the introduction of the development initiatives, and the resultant increase in PREO activities, significantly reversed this trend, the PREO-based developments have exposed the absence of a structured career path in Irish RIs for researchers wishing to focus exclusively on research.

As such, highly trained actors are leaving research positions to advance their careers. A RI respondent commented that:

> "...being a professional researcher who is focused one hundred percent on research is not possible...for someone in their late twenties to continue in research it is very difficult. There are very few permanent research posts, or pensionable positions. Things are too temporary for someone to settle down in...so people get out of research and move into companies, or into lecturing...those that leave have to be replaced, and it basically restarts the system" (RI respondent 5, interview).

This issue has major implications for the bio-sector's ability to develop and retain a specialised labour pool. While this issue has been acknowledged by the Government, no developments to address this issue have yet occurred (Forfás, 2008).

Several PREO-based respondents commented that this scenario will intensify, as the Government's on-going skills development drive, which has also sought to increase the supply of PhD graduates to the bio-sector, is not part of a coordinated programme. Essentially, these skills developments are being targeted in isolation, while little effort is also being taken to address the lack of science uptake in secondary schools, as well as

existing downstream sector weaknesses.

Finally, several PREO respondents commented that the absence of national and/or international academic or industrial placements for Irish academics is a critical issue undermining the development of key skill sets, and the diffusion of tacit and codified research information, commercial knowledge and spillover developments throughout the bio-sector.

Perversely, industrial placements are key elements in undergraduate biotechnology courses, and greatly influence the commercial orientation of students by allowing them to place their academic learning into practice in an industry setting in order to acquire significant levels of tacit knowledge and exposes them to the demands, requirements and pressures of a commercial environment. One RI-based respondent with undergraduate placement experience in both the US and Irish bio-sectors commented that the placements demonstrated:

> "...that biotech isn't just research...I worked in a lab[oratory] in America and saw the research side. I was working in a diagnostics lab in Dublin where I saw the production side of things up close, so I learnt it's not all research based" (RI respondent 6, interview).

The absence of placements therefore restricts the level of industrial experience and know-how academics have, which inhibits their ability in dealing with, and entering into, commercial activities. Respondents noted that this issue initially developed due to the limited resources available to both PREO and downstream actors in the pre-initiative bio-sector, as well as due to the presence of structural rigidities, i.e. pre-initiative employment contract rigidities and administrative structures dissuaded actors from entering into placements. Despite the on-going PREO infrastructural developments, no defined programmes have formed and/or been introduced, while the structural rigidities remain. Additionally, respondents commented that the increased funding levels available to academics have unintentionally discouraged researchers from seeking such placements, or from seeking 'work' sabbaticals.

8.2.2.1.3 Cross disciplinary structural weaknesses

The post-initiative RIs represent the first development of cross disciplinary institutional structures in the country's PREOs. However, their ultimate effectiveness as bridging mechanisms will be determined by how they address existing/on-going academic norms and values in the different 'parent' departments, schools, and universities.

Established 'mismatches' between the discipline-specific structures and cultures of the different RI actors are impacting on their forms and functioning, i.e. discipline-specific values, cultures, reward structures, budget and management systems mean intangible 'walls' have formed among the different elements of the RIs.

Additionally, despite significant developments having occurred in the country's IoTs and research hospitals (RHs), many respondents commented they essentially remain outside of the on-going sectoral developments and activities. Indeed, the research elements of the country's hospitals are only integrated into RI activities in the Greater Dublin Area (GDA) through the Dublin Molecular Medicine Centre. This issue was identified by many respondents as restricting potential networking and commercialisation opportunities across the bio-sector.

8.2.2.1.4 The weak commercial orientation of administrators, academics and students

The commercial orientation of academics and administrators in the pre-initiative bio-sector was poor. Despite the more pronounced and defined commercial emphasis that the on-going initiatives are seeking to embed in the PREOs, respondents commented that the commercialisation skills among PREO administrations remain very limited, and continue to undermine commercial developments from PREOs. Several respondents commented there is a clear need for "…more trained people [in administration positions], as a lot of the [current] people don't have real formal training" (Investment respondent 1, interview).

Essentially, the long term absence of a defined commercial focus to PREO-based activities means no commercialisation culture exists for on-going initiatives to build upon, i.e. a time lag has developed between the introduction of the post-initiative supports and their ability to address these issues.

This is proving difficult to address due to the presence of a distinguishable 'age gap', as identified by many respondents, between commercially-orientated academics and those who are not. This issue exists due to the presence of different employment contracts types and when these contracts were signed. Pre-initiative PREO promotion procedures placed no weight on licensing or commercial developments, only on publishing. While these procedures have now been amended to include patenting in promotion evaluation processes, this is a relatively recent development.

Despite the introduction of the more advanced PREO commercialisation procedures and supports, the limited commercial know-how among the pre-initiative PREO academics remains. A number of senior academic respondents commented that their desire to initiate commercial activities is restricted by their limited commercialisation/business acumen. One such respondent commented that "if something did come out of some research, I wouldn't know where to start...I haven't done a patent, and I'm not sure what is involved. There are set avenues you take and all that, but I'm not too sure about them" (University respondent 3, interview).

Indeed, a TTO respondent commented that this 'age' divide has impacted on commercial developments:

> "We've had stuff slip through our fingers, stupidly so. One guy published something that should definitely have been patented...he hadn't been to any of the commercial courses we'd run. I told him all he had to do was wait about two weeks for the patenting paperwork to be filed and then he could publish it all...but he didn't know anything about what I spoke to him about...we've really had to fight sometimes to get people up-to-date on these things" (TTO respondent 1, interview).

An investor respondent noted the importance of commercial know-how:

> "If [as an academic] I walked up to you and said that I want you to put €50 million into a company I'm creating, but I've never run a business before. I've never sold one, never taken one from basic stage to something where someone is willing to buy it. If I came to you like that, you're not going to give me €50, let alone €50 million. You'll only give it to people with experience. I mean, how else can you justify it?" (Investor respondent 1, interview).

Aside from inhibiting commercial developments, this limited commercialisation acumen also feeds into the commercialisation culture in which current students develop and emerge from, i.e. the poor commercial orientation and skills of senior academics will impact on the commercial orientation of the bio-sector's future researchers and industry employees, which will then feedback into future sectoral developments.

Indeed, the commercialisation elements in current PREO under- and post-graduate education programmes are minor. Undergraduate degree courses predominantly focus on educating students in the technical aspects of biotechnology/life sciences to prepare them for industry-based technical jobs following their graduation, while post-graduate studies overwhelmingly focus on research activities. As such, students enter their professional careers with very limited experience and knowledge on developing commercially orientated research activities, patents, and/or licensing agreements.

A bio-firm respondent commented that, optimally:

> "[industry actors would] like to see a module dedicated to the business world and commercialisation, a bit like the MIT [the Massachusetts Institute of Technology] model where everyone coming out with a masters or a Ph.D. knows what they are doing with regards their IP, and can talk the talk...but this doesn't exist" (Bio-firm respondent 8, interview).

Several respondents commented that this skills issue is a major stumbling block to the long-term development of commercial concerns in the indigenous bio-sector, as commercial expertise plays a key role in the development of commercially viable research, and in commercial developments.

8.2.2.1.5 PREO commercial support and intermediary actor weaknesses

Despite noticeable developments having occurred in the ILOs and TTOs of the PREOs due to the on-going initiatives, many respondents commented that significant issues remain.

Wide discrepancies exist amongst the commercialisation policies and supports of the individual PREOs, i.e. similar, though different agreement forms and requirements exist, which several respondents typified as being poorly designed. These issues create a level of uncertainty that undermines collaborative, inter-actor and inter-institutional alliances.

An investment respondent commented that "the business side [of the PREOs] hasn't grown as fast as the science aspect...technically they are up there, but commercial management in Universities is still very poor" (Investment respondent 2, interview), i.e. the drive to commercialise PREO-based research has not been matched by a corresponding increase in commercialisation supports. Indeed, a TTO respondent commented that the existing commercialisation supports "are just hitting the bare minimum level really...they are not aiming high enough, and it's all too piecemeal too" (Technology transfer respondent 3, interview).

A key issue is the absence of a uniform Intellectual Property (IP) policy among the PREOs, despite the implementation of up-to-date patent and IP policies and the drafting of an PREO IP code of practice by SFI and EI (along with other agencies) in 2005. An investment respondent, with extensive experience of the US bio-sector, commented that "...there is virtually no experience in this area [IP] in Ireland at present." This is "turning people away, all because of the risk levels they perceive" (Investment

respondent 1, interview), which contributes to an international perception of Ireland having weak IP policies.

Additionally, the bio-sector's intermediary actors are essentially restricted to EI's incubators (innovation centres). An investment respondent commented that these incubators "are full, but they aren't real incubators...if you compare [them to] what's available in other countries" (Investment respondent 2, interview), due to the relatively limited nature of their facilities and the limited provision of business and management development services and supports. This respondent also commented that the incubators "...were filled on a first come, first serve basis. No quality checks took place. So there are projects in these places that will never succeed...and that means viable projects are left out" (Investment respondent 2, interview).

Another key issue, as identified by many respondents, relates to Enterprise Ireland's Biotechnology Directorate (EIBD). EIBD has no direct on-campus activities at two universities, the National University of Ireland, Maynooth (NUIM) and the University of Limerick (UL), nor at any of the country's Institutes of Technology (IoTs) or RHs. This scenario exists despite many of these PREOs being engaged in biotechnology/biotechnology-related research programmes and, in relation to NUIM, UL, and Athlone IT, having on-campus biotechnology/biotechnology-related RIs. This issue has impacted on the commercial-orientated research activities in these PREOs, and also on their ability to develop commercial alliances.

This scenario originated with the establishment of EIBD's predecessor, BioResearch Ireland, in 1987. BioResearch Ireland's five RIs were established in the country's existing five university locations, yet UL and NUIM were established, respectively, in 1992 and 1997. Following EIBD's establishment in 2003, the pre-existing facilities and arrangements were continued, only their commercial focus was augmented.

One investor respondent commented:

> "BioResearch Ireland should have been organised around a central point rather than being spread throughout the universities and ignoring Maynooth and Limerick. It has to have hurt those universities...if someone wants to spin-out a company in either place, where do they go?" (Investment firm respondent 1, interview).

A university administration actor respondent from one of these universities commented:

> "We've argued with [EIBD] for support, but for a long time the response has been to use the person in XX [a nearby EIBD-supported university]. But there is a conflict of interest there. If [an EIBD representative in a nearby EIBD-supported university] has two projects, one from their own academics and one from us, the XX [based] project will get precedence. The EIBD people are…fully aware of the awkward situation, but there is a conflict of interest. If someone worked here for a day or two a week, at least they would be here and we could talk to them. But EI have said the only way to get someone on campus is to have significant activity. So it's a chicken and egg scenario, and it does cause problems in trying to get stuff out to interest potential collaborators" (University respondent 2, interview).

A TTO respondent in one of the two Universities commented that the absence of EIBD had impacted on the level of commercial developments that had originated from his university: "...up to 2000, the entire university had one patent...when it came to our first patent, we had no structures in place" (TTO respondent 1, interview). Various respondents in these PREOs commented they had essentially adapted to the on campus absence of EIBD, yet they still view this scenario as being a significant weakness undermining potential commercialisation developments, i.e. "...the physical presence of EIBD is required" (TTO respondent 4, interview).

8.2.2.1.6 Limited commercial 'marketing' by PREOs

PREOs in the leading international bio-sectors proactively mine for commercially viable research, in the context of extensive commercialisation procedures and supports, and also seek suitable commercial actors with which to engender such developments. In contrast, the TTOs and ILOs of Irish PREOs are characterised by commercial actor respondents as being "full of traditionalists who won't actively mine for information" (Bio-firm respondent 6, interview).

A PREO-based respondent commented that, in relation to the commercialisation pressures deliberately engendered by the on-going initiatives, it was vital that the PREOs had "people who can interact with companies and who have a very clear commercial focus...who can go out then and sell the concept, sell the products...[but] they simply aren't there" (University respondent 6, interview). An investment respondent commented that the PREOs "are not putting in enough human resources to do all that's required, finding the research, preparing it, and then go out on the streets, so to speak, to sell it" (Investment respondent 1, interview).

Several bio-firm actors, who had previously sought to develop alliances with Irish academics, commented on their continuing frustration at the significant restrictions and difficulties they face in accessing information on the completed and on-going commercially viable research programmes/projects of the PREOs. The PREO have their

own research database on the projects being conducted by their full-time academic and postgraduate researchers, yet they are not uniform in content or presentation, while commercial respondents commented that the information they contain is either too academically orientated, or not specific/detailed enough to be useful for their non-academic queries.

These issues are impacting on possible commercial alliances. A bio-firm actor commented that his firm often finds interesting research by accident: "...many times we have stumbled on research that would be carried out in hospitals, or in Universities, that would certainly be valuable to us" (Bio-firm respondent 4, interview), while another bio-firm respondent stated that "we [are] getting most of our information from the US" (Bio-firm respondent 9, interview) directly as a result of this issue.

8.2.2.2 Bio-firm weaknesses

The bio-sector's pre-initiative bio-firms are engaged in diagnostic-based activities that were mainly derived from non-Irish IP. As such, they engage in limited research activities, and have established very limited linkages with other sectoral actors. Additionally, despite the on-going sectoral development initiatives having facilitated the development of more advanced 'Genentech template' bio-firm developments, the development agencies have focused on engendering diagnostic and therapeutic bio-firm developments.

As a result of their business models, both pre- and post-initiative bio-firms are characterised by relatively low investments in research, indeed an investment paradox can be observed among the pre-initiative bio-firms. This means that significant inter-actor exchanges of formal information/knowledge and of science/technology competences between bio-firms and PREOs, and downstream actors are not occurring.

Overall, the limited entrepreneurial character of the bio-sector's bio-firms is one of the most serious issues influencing its development trajectory. Yet, additional issues can be identified in the character of the indigenous bio-firms, these include:

- the majority of the bio-sector's pre- and post-initiative bio-firms are engaged in pharmaceutical-based activities, i.e. therapeutics and diagnostics. Yet, a mass of bio-firms in such areas is forming in the international bio-sector. This means that the Irish bio-sector is essentially seeking to compete in an already crowded

market place,

- there is a lack of advanced bio-firm activities, in particular drug development activities, in the bio-sector. This is a key weakness, as the bio-sector is open to possible 'lock-in' developments if shock/chance events occur in the international bio-sector. Additionally, this issue restricts the bio-sector's ability to attract more complex actor and skill types, e.g. advanced TNC research operations, which will inhibit future spillover developments,
- the lack of commercial activity means there is a real threat that the advanced level of PREO-generated IP may ultimately result in what one academic respondent termed 'IP flight' to bio-sectors with more advances capabilities and activities, due to the restricted commercial avenues that presently exist in the bio-sector, and
- the limited range of sectoral activities and the relative absence of successful product commercialisation mean the indigenous bio-sector has a very limited international image, outside of the PREO-based developments, which undermines the ability of commercial actors to enter into alliances with actors in the hub bio-sectors.

8.2.2.3 Entrepreneurial development skills and investor actor weaknesses

The indigenous bio-sector has a significant lack of entrepreneurial experience and know-how. An investment respondent stated:

> "[the bio-sector] requires people who have made it as entrepreneurs and who have been successful, and entrepreneurs who have not been successful, who have failed, in order to get that level of awareness...we don't have the history of this type of thing here, we don't have that depth of experience to draw from" (Investment firm respondent 2, interview).

This issue is one of the biggest tasks/challenges facing the bio-sector's development. It is crucial that bio-firms optimally develop their business side to an internationally competitive level, as accessing indigenous funding sources will become increasingly competitive as more commercial entities develop, while suitably developed business elements are fundamental requirements in accessing non-Irish funding sources. An investment respondent stated that "...a great idea is nothing but a great idea without the right experience and skills to develop the idea into a firm. This is when an entirely different skill set is required...and these skills are missing in Ireland" (Investment respondent 1, interview).

Several respondents noted that the bio-sector's demand for these skills greatly outstripped their supply, as evident after Élan's restructuring in 2003; Élan halved its global work force in 2002, releasing many highly skilled personnel, many of whom had extensive management skills. This resulted in a massive bidding war among prospective sectoral employers, as bio-firms sought to access their skills sets (Technology Ireland, 2005).

Additionally the indigenous bio-sector's investor coverage is essentially limited to public sponsored VC funding, i.e. a very limited range of investor actor types exist. This limits the type of commercial developments that can occur in the indigenous sector, as different investor actor types have different risk profiles. Many sectoral respondents commented that the limited variety and public nature of investor actors is feeding into and reinforcing the post-initiative development focus on diagnostic and therapeutic firms.

Several academic and bio-firm respondents stated that, in seeking to by-pass the lack of investor variety, they had sought investment funding from non-Irish sources. Yet, the limited track record of commercial developments in the bio-sector means such investors remain unconvinced about the bio-sector's commercial potential.

Furthermore, possible exit strategies for investor actors are limited in the indigenous bio-sector, i.e. alliances with TNCs and stock market floatations are undermined by the relative absence of TNC involvement in the bio-sector, while market floatations are also very limited. Investor respondents commented that the Irish stock market is limited in size and is risk averse due to the unproven nature of the bio-sector, while alternative stock market options are limited, i.e. US stock markets are ever more circumspect about the commercial potential of bio-firms due to the continuing consolidation and the maturation of sectoral activities, while European stock markets which do accept bio-firms, such as the London-based FTSE, and the Frankfurt Stock Exchange, were characterised by sectoral investment actors as only being uninterested in investing in EU-based bio-firms when US VC interest is present.

Essentially, an investment paradox exists, i.e. the limited commercial developments and exit strategy options in the Irish bio-sector deter potential investors from entering an 'unproven' bio-sector, while limited investor coverage, due to the perceived risks and

costs in developing commercial developments, restricts commercial developments.

8.2.2.4 TNC-related weaknesses

The IDA Ireland's efforts to embed/seed TNC R&D biotechnology-orientated operations into Ireland have had limited, yet important success, i.e. TNCs, such as Genzyme and Wyeth, have located R&D operations in Ireland. Their involvement in sectoral activities, however, is very limited as they are essentially R&D 'branch plants' that have little autonomy over their research programmes. Furthermore, their activities are characterised as being close to the end of the applied research phase/at the beginning of the product development process, which means their activities are too advanced to develop linkages with PREOs.

Despite the adoption of more biotechnology-related activities in the Irish TNC operations, which reflects an international trend among TNCs, a TNC respondent stated that sectoral activity remains too limited 'across the board' for significant TNC alliances to develop with sectoral actors.

An investment correspondent noted that, even with the increased level of PREO-based research activities, "the equipment base in Irish PREOs...isn't up to the pace of the TNCs" (Investment respondent 2, interview), which, allied to the limited research autonomy of the Irish-based TNC operations, means that few research-based alliances have developed.

Additionally, PREOs are not optimally addressing the skills requirements of the TNCs. An analysis of the skills requirements of GDA-based TNCs by van Egeraat and O'Byrne (2010) highlighted a number of national issues, particularly the presence of a mismatch between TNC skills requirements and the relevant PREO courses. This is a developing and deepening issue, which particularly relates to the increased adoption of biotechnology-related practices in the TNCs (Forfás, 2003).

In relation to indigenous bio-firms, pre-initiative bio-firms have little to attract major TNC interest, while the post-initiative firms have developed very limited TNC alliances due to their current state of development. An investment actor noted that TNCs will:

> "...only start getting interested [in indigenous bio-]firms when they get near the clinical trial stage, but...many products can't be brought up to this point...because the [bio-] firms don't have the resources or finance to do so" (Investment respondent 1, interview).

This means that indigenous bio-firms are effectively caught in a TNC-related development paradox, i.e. to attract TNC attention they must first develop substantial R&D programmes, yet they require TNC involvement to develop such programmes.

Ireland's ability to attract in more advanced TNC activities is also being undermined by the country having become an expensive location for businesses as a result of the 'Celtic Tiger' economy. Wage costs, particularly in the GDA, have risen, while a range of non-pay costs, including energy, telecommunications, insurance, and waste management costs, have also increased significantly to impact on Ireland's competitiveness, relative to other EU countries. These issues were significant contributory factors by the decisions of Dell and Pfizer to close/re-size their Irish operations (Cassidy and O'Brien, 2005; van Egeraat and O'Byrne, 2010).

TNCs are sensitive to regional differences in labour costs, indeed respondents commented that the more traditional and cost-sensitive segments of the Irish Pharmaceutical sector are facing increasing competition from low cost R&D locations, i.e. India and China. Respondents commented that issues relating to the strength and quality of IP protection in these countries are currently discouraging TNCs from re-locating to these countries, but that "...it's really only a matter of time before they sort out their IP problems and these [Irish-based TNC] elements move" (TNC respondent 3, interview).

Ireland's ability to retain and attract FDI activities also faces serious infrastructure-related threats relating to the supply of adequate and affordable water and wastewater services, crucial requirements for TNC production processes due to their requirements for access to large quantities of fresh water, and suitable wastewater facilities (van Egeraat and O'Byrne, 2010; Forfás, 2008).

Serious issues exist, or are forecast to develop in relation to these services, nationally. In relation to the main TNC locations, i.e. the GDA, and the Cork and Galway City regions, Forfás (2008) noted that Dublin/the GDA is expected to experience water supply and waste water treatment shortages by 2013. On-going and planned infrastructural developments are ultimately expected to be insufficient to fully cater for future increases in demand by enterprise in the region. Galway will face a water supply shortage by 2013, no future developments are planned, while Cork is also expected to

begin reaching its full water and waste water infrastructural capacity by 2018 (Forfás, 2008; Dublin City Council 2009a, 2009b; van Egeraat and O'Byrne, 2010).

Additionally, Ireland has a limited wastewater infrastructure. Dublin City's wastewater infrastructure focuses solely on the Ringsend Wastewater Treatment Works. Even with the completion of a planned upgrade, maximum capacity will be exceeded by 2014. Galway is already experiencing serious waste water treatment issues, while Cork is expected to exceed its waste water treatment capacity by 2013. No future developments are planned for either city (Forfás, 2008; Dublin City Council 2009a, 2009b; van Egeraat and O'Byrne, 2010).

In relation to contaminant waste disposal facilities, a key requirement for bulk manufacturing TNC operations, the Cork region is adequately provided for, yet no contaminant waste incinerator exists in the GDA. The vast majority of contaminated material produced by GDA-based TNCs is exported to the UK for disposal, which increases operation costs considerably. No dedicated industrial waste incinerator developments in the GDA or in Galway are currently planned (van Egeraat and O'Byrne, 2010).

8.3 SECTORAL DEVELOPMENT POLICY PROPOSALS

The analysis of the various strengths and weaknesses present in the indigenous bio-sector demonstrates that while the on-going public initiatives have facilitated important sectoral advancements, they have not counteracted the bio-sector's existing path dependence and development trajectory.

This issue reflects the Irish Government's limited understanding of the bio-sector's complex structure. Essentially, the government has approached the bio-sector's development as if its value chain was a traditional linear structure, i.e. the PREO-centred developments are viewed as automatically/organically driving downstream developments, such as attracting in more complex TNC activities and private speculative investor actors.

Many sectoral interview respondents commented that there is no guarantee these elements will automatically appear, as sectoral activity levels are too limited for such developments to emerge 'organically' for the foreseeable future. This is demonstrated by the failure of the post-initiative commercial developments to offset the relative absence

of an entrepreneurial climate among sectoral actors.

Essentially, the scale and depth of the inter-related weaknesses are proving difficult for the on-going initiatives to fully address, as their current form cannot address various features of the pre-initiative bio-sector which remain deeply engrained in the characters of the bio-sector's actors and their structures/infrastructures, e.g. the limited information spillover developments that occur in key areas of the bio-sector's value chain due to previous sectoral limitations undermining the development of an interactive environment. This means that entrepreneurial and innovative developments throughout the bio-sector's value chain are restricted, as the on-going weaknesses create and reinforce negative feedback inputs which undermine the bio-sector's development trajectory.

The limited entrepreneurial and innovative developments occur due to the absence of a defined or co-ordinated policy programme that targets the entire bio-sector's development as a whole, as well as on-going issues with policies that impact on the wider industrial base. These include**:**

- the lack of co-ordination between the Government's industrial and STI policy strands, i.e. both strands exist parallel to each other, with no co-ordination and/or complementary supports being present;
- the reactive and top-down nature of Government initiatives, i.e. their formulation does not pre-empt development trends and/or issues which could emerge due to their introduction, and;
- the absence of the concepts of networks and clusters as defined aspects of current industrial policy despite many reports since the early 1980s calling for their introduction, and their entry into the vernacular of Government agencies over the last 10 years.

Furthermore, the continuing focus and dependence of the Irish economy on foreign direct investment (FDI) and the limited research and innovative activities of the country's indigenous industrial-base means that an innovation paradox remains among Irish PREOs and indigenous industrial firms, i.e. the limited abilities of PREOs to engage in or diffuse commercially-orientated research activities, and the limited absorptive capacity or ability of indigenous firms to engage in such activities.

As such, an advanced commercialisation mindframe and support infrastructure in the wider industrial base does not exist, which means that innovative developments in the indigenous bio-sector are essentially an anomaly. This issue also inhibits potential cross sectoral developments, and feeds into and compounds the poor entrepreneurial environment found in the bio-sector.

Overall, these issues demonstrate that a comprehensive coordinated, long-term and adaptive systems-based policy framework which transcends business and election cycles is required to replace the current piecemeal policy approach, and to optimally address the complex, inter-related and wide range issues which are present in the bio-sector. Such a framework must seek to build upon and advance the bio-sector's existing strengths, in a systematic manner, so as to facilitate inter-actor synergies and spillovers that engender a more advanced and pronounced entrepreneurial and innovative environment.

Essentially, policy developments must focus on engendering positive externalities in order to drive and optimise the bio-sector's path dependence and development trajectory. Positive externalities are required to build upon existing systemic strengths and address existing systemic weaknesses through positive feedback inputs. Different supports play different roles in the technological and regional dynamics of a system, yet they are mutually determined in a complex web of circular cumulative causation which continuously alters through place/system specific feedback.

Key determinants of the bio-sector's positive development trajectory will be entrepreneurship and innovation, i.e. the development of new firms, products and processes, which will create positive feedback inputs that reinforces a bio-sector's evolution by addressing issues such as lock-in and technological discontinuities. Such developments are facilitated and determined by the presence of an entrepreneurial support 'ecosystem' that both facilitates and encourages innovative developments. The factors which characterise an ecosystem are fundamentally linked.

The development of a comprehensive, coordinated, long-term and adaptive systems-based policy framework will require closer collaboration between the Department of Enterprise, Trade and Innovation (DETI) and the Department of Education and Skills (DES), in order to coordinate the Government's innovation and industrial policy strands, and to integrate the activities of all Government agency actors which currently impact on the indigenous

bio-sector.

Yet, the optimal formulation and implementation of such a complex framework should occur through consensus building among all relevant public and private sectoral stakeholders, including local authorities, chambers of commerce, business associations and enterprise boards.

In the context of the bio-sector's current state of development, and the established nature of the Irish Government's structures and policies, a public/private dialogue process would initially require substantial public actor leadership, under the auspices and guidance of Forfás and EI, so as to introduce the suitable interactive dialogue structures that would evolve with sectoral developments and would ultimately engender a collaborative, private actor driven entrepreneurial environment.

The participation of the bio-sector's key public and private actors is crucial in facilitating the emergence of a rapidly adaptive policy environment that allows the bio-sector to quickly and suitably respond to possible/potential future developments in the international bio-sector. Examples of such developments include:

- the potential opportunities that the on-going stratification of the downstream end of the international bio-sector's innovation process may present in the context of the increasingly niche activity focus of bio-firms and the increasing adoption of biotechnological practices by TNCs internationally, and;
- the potential of Genomics to revolutionise all aspects of the bio-sector and expand the reach and impact of biotechnology into areas never previously thought possible by replacing/undermining existing industrial paradigms.

Additionally, a defined regional emphasis must also be developed to tailor initiatives to optimise the idiosyncratic development trajectories of the main geographic concentrations of the bio-sector's activity, i.e. the Greater Dublin Area, the Galway City area, and the Cork City area. This would require an increased degree of co-ordination between the regional branches of development agencies and local authorities must also develop, so as to create a 'collective' vision for regional industrial and economic development.

However, developing a regionally focused public/private dialogue process will be a

challenge as few established public/private actor dialogue systems presently exist. National consultation procedures with non-Government actors, such as academic researchers and business actors, are limited to the on-going national wage agreements, consultation processes in the development of foresight papers, and private actor lobbying. Additionally, no defined autonomous regional Government structures currently exist.

As such, the development agencies, local authorities, chambers of commerce, business associations and enterprise boards should prepare a joint statement that states the intent of sectoral development initiatives.

The following 'hard' and 'soft' policy suggestions are derived from the findings of chapters 5, 6 and 7, and are presented in the context of the entrepreneurial and innovative support 'ecosystem' framework template presented in chapter 3. In essence, these suggestions represent complementary aspects of an interactive, multi-faceted, systems-based support ecosystem that seeks to build on underlying strengths of the indigenous bio-system, and to engender the conditions that facilitate and drive entrepreneurial and innovative developments among all areas of the bio-sector's networked structured, nonlinear value chain, to create a self-sustaining system that optimises its development trajectory.

8.3.1 Knowledge base infrastructure, resources and skills

The quality and character of the research capabilities, resources, skills, and (sticky) knowledge sets of a bio-sector's PREOs are fundamental elements in engendering the synergy-based processes that will drive its trajectory. These elements ultimately determine a bio-sector's commerciable research activities, and its bio-firm and biotechnology-derived product and process developments.

The majority of the bio-sector's strengths have been seeded in the country's PREOs. The following policy suggestions seek to build upon the substantial infrastructural and skills developments introduced by the on-going initiatives, and to address existing issues identified above in section 8.3. These include:

- the clear division of activities between PREO actors, i.e. the various university departments, and their associated research institutes (RIs) are effectively 'separate' entities, while the Institutes of Technology (ITs) and the Hospital RIs

are essentially removed from on-going developments;

- the limited commercial orientation of academics and administrators due to the presence of a restricted entrepreneurial culture, and;
- the uncertainty of the long-term ability of PREOs to retain key skills, due to the absence of researcher career paths.

In order to achieve a critical mass of research activities, inter-institutional collaboration among all the PREO actors needs to emerge. This requires public initiatives to address the existing infrastructural and resource issues among PREO actors that restrict inter-actor alliances and tacit knowledge exchanges. Public investments, through the PRTLI, must also seek to improve and expand the research capabilities of the IoTs and Hospital RIs, so as to integrate them into the commercial research-related activities of the bio-sector. This is particularly pertinent due to the pharmaceutical orientation of the bio-sector.

Essentially, more holistic structures should be sought in the PREOs, to remove existing structural and institutional divisions, i.e. a more integrated, intra- and inter-departmental 'spectrum' like structure should be developed which introduces integrated departmental and institutional structures and supports, and compliments the different research and teaching activities of the PREOs. Such structures would facilitate the more efficient development and use of PREO infrastructures, resources and skills by improving the inter-institutional mobility of researchers and technicians.

However, introducing more integrated intra-PREO structures would require a significant restructuring of the existing structures and facilities of the country's PREOs, while it would also be important that such developments should retain the diversity of the different PREO institution types. As such, the design and implementation of conjoined administrative structures and infrastructures could occur over a long-term, phased process developed through a consultation process with all the relevant actors and supported through public actor regulatory alterations and funding supports (Forfás, 2004).

Furthermore, the current policy focus on facilitating increased applied research activities among PREO actors must be expanded to include basic research activities. Basic research advances the scientific/technological knowledge base of PREOs and is a key

requirement for the long-term development of a complex and varied 'world class' research base and downstream sectoral developments, as it also plays a central role in the development of a highly skilled workforce, thus directly contributing to new technological and entrepreneurial developments. As private actors avoid basic research activities due to their exploratory, less definable nature and higher risk profile, public funding is therefore crucial.

In relation to the on-going skills development activities of the PREOs, it is vital that suitable under- and post-graduate educational courses in all biotechnology-related subjects are introduced. Such courses should be developed within a comprehensive skills development programme, which should feed into secondary level education course developments (this area is outside of the remit of this study), so as to respond to and meet the existing and future skills demands of all downstream sectoral actors, including bio-firms and TNCs. This suggestion echoes the Government's Strategy for Science, Technology and Innovation (2006-2013).

Optimally, such a skills development programme should be informed by the public/private consultation processes in order to optimally tailor them towards the demands and needs of the bio-sector's actors, and should link in with the information disseminating structures and placement programmes proposed in section 8.3.4, as well as efforts to engender a pronounced sectoral entrepreneurial culture.

A key requirement for the bio-sector's development trajectory is the ability of its PREOs to retain and develop a skilled labour pool. A key issue undermining such a development is the absence of a defined career path in the RIs. This issue must be addressed to ensure the optimal development of the PREOs and the bio-sector. Addressing this issue will require the long-term development of suitable structures, which could potentially be developed through the introduction of integrated PREO structures, as suggested above. Such structures should include a rigorous internationally competitive selection process, including competitive research fellowships, to ensure that a high quality level is developed and maintained (Forfás, 2008; Delerue and Lejeune, 2011).

Additionally, the TFF's focus should be expanded to attract skilled Irish researchers back into indigenous PREOs so as to facilitate increased spillover developments, and feed the development of a national network promotion programme. This would be dependent on

an increased level of sectoral activity, as well as the presence of a defined researcher career path. Additionally, integration strategies should be developed to complement the TFF so as to better integrate such academics entering existing PREO structures, as well as to address potentially belligerent reactions from existing academics (Anderson et al., 2004).

The infrastructural recommendations presented in this section are directed towards the HEA, with respect to the agencies and funding programmes under its aegis, and the Departments of Education and Finance. The suggested skills recommendations are directed towards the relevant bodies under the aegis of the DES.

8.3.2 Entrepreneurial infrastructures, resources and skills

The on-going sectoral development initiatives have increasingly focused on facilitating commercial developments from the increased activities of the PREOs. These efforts, in combination with the introduction of commercialisation supports, have facilitated the emergence of post-initiative bio-firm developments, which has augmented the commercial orientation of the bio-sector.

However, the overall level of entrepreneurship in the bio-sector remains restricted due to:

- the general absence of an entrepreneurial mindframe among PREO academics and administrators;
- the still limited nature of the recently introduced commercialisation supports;
- the limited availability of business development actors/skills;
- the restricted nature of the post-initiative bio-firm developments, and;
- the established innovation paradox among the pre-initiative bio-firms caused by the very limited nature of the pre-initiative sector.

The engenderment of vigorous entrepreneurial and innovative sectoral activity will ultimately be determined by the development of a sectoral entrepreneurial support infrastructure and the psychological and/or social characteristics of its actors; entrepreneurship is an endogenous process, a learned set of guidelines that co-evolves with a region's business activities and supports, creating a system specific culture (Compete, 2005; Anderson et al., 2004; Owen-Smith and Powell, 2007; Engel and Del-Palacio, 2011).

A more complex, integrated and proactive commercialisation support infrastructure must be developed to both facilitate and drive entrepreneurial developments throughout the bio-sector, particularly among PREO academics and administrators and the pre- and post-initiative bio-firms. It is important that such an infrastructure focuses on quality, not quantity, and that it avoids the development of protectionist elements that reduce entrepreneurial and innovative pressures in the bio-sector, e.g. the introduction of direct/indirect subsidies. Such an infrastructure must also support entrepreneurial experimentation in order to facilitate the emergence of a more complex and varied bio-sector. These developments must also be extensions, not replacements, of existing supports and should actively seek the ultimate development of a range of privately organised supports, e.g. private VC (Owen-Smith and Powell, 2007; Engel and Del-Palacio, 2011).

The following suggestions essentially build upon and expand current PREO structures and capabilities to develop a comprehensive support structure. Many of the following suggestions are directed towards EI.

Significant issues and differences exist in the depth and range of the commercialisation capabilities and resources of the PREOs' TTOs and ILOs. Additionally no uniform IP or licensing regimes exist among the PREOs, while database format differences and the limited advertising of PREO research activities are inhibiting the development of downstream alliances. Furthermore, Enterprise Ireland's Bioresearch Directorate (EIBD) has no direct on-campus activities at the National University of Ireland, Maynooth (NUIM), and the University of Limerick (UL), while no direct supports have been developed at the IoTs or the relevant Hospital RIs.

In order to address these issues, EIBD should be remodelled to form a more comprehensive, integrated national commercialisation structure, i.e. on-site facilities should be established at all existing (and future) PREO actors so as to engender a more defined and pronounced commercialisation orientation to their activities.

Parallel to the proposed programmes in section 8.3.1 that support the development of basic and applied research programmes and the integrated PREO structures, EIBD should introduce advanced commercialisation procedures and supports, including uniform IP and licensing regimes, that integrate with the existing structures, so as identify and optimally support the exploitation of commercially viable research. Their

long-term aim should be the seeding of relevant skills and competences among PREO administrators, ILOs, TTOs, academics and students, in alliances with the relevant hard commercialisation supports (detailed below), in order to facilitate and drive commercial developments with the wider sectoral system.

A possible alternative to establishing on-site EIBD facilities, in the context of the limited PREO-based commercial activity and the lack of uniformity to their commercialisation procedures, is the development of a central entrepreneurial support structure that all PREOs can access. Such a structure, which would fall under the supervision of EI (EI already hosts the BiotechnologyIreland website), would complement and build upon existing support structures through providing up-to-date and standardised IP, licensing and legal supports.
Regional elements to such a service could eventually be established, as, in the context of the bio-sector's on-going development trajectory, the requirements of the individual PREOs would become increasingly idiosyncratic. Such a service could be also expanded to address the limited level of service and supply firms present in the bio-sector.

Furthermore, a centralised database, detailing standardised and up-to-date information on PREO-based research programmes, could also be developed so as to improve the ability of commercial actors to access detailed information on on-going and completed PREO research programmes.

In relation to the bio-sector's bio-firms, various initiatives must be introduced to coordinate and advance the assortment of entrepreneurial infrastructures and resources which currently exist.

The limited investment levels of indigenous bio-firms in research is one of the most serious issues influencing the bio-sector’s ongoing development, particularly through restricting the formation of substantial up- and downstream inter-actor alliances/networks. The sectoral development initiatives must focus on boosting the bio-sector's entrepreneurial 'pressure', as despite the new RIs having generated many long-term benefits, their public nature means they will fail to develop the local actor synergies associated with commercial/private entities.

Existing bio-firm development supports and initiatives are overwhelmingly focused on the post-initiative bio-firms. This focus must shift to address the poor relative state of development and activities of the pre-initiative bio-firms in order to deepen the depth and activity variety of the indigenous bio-sector, this proposal relates to section 8.3.5.

Several respondents commented that an opportunity exists for the Government to provide funding to allow the pre-initiative bio-firms develop research programmes. Yet, such funding could potentially distort the market place through becoming an indirect subsidy. As such, such supports should be modelled on EI's existing R&D funds, which seek to enable small to medium enterprises (SMEs) develop their innovation capability and absorptive capacity, so as to allow SMEs develop their research activities/capacity and business structures to a level where collaborations with other actors becomes feasible.

This approach would require a long-term focus and the introduction of suitable business development and technical supports that would address the conservative business models and limited innovative competences and resources that characterise the pre-initiative bio-firms. Optimally, such aspects should be addressed through establishing tailored development consultancy services that allow the bio-firms access optimised research and commercial resources and skill sets, so as to increase their absorption capacity in such areas.

Parallel to such developments, a TFF style programme or consultancy service should be developed to address the key areas speculative investors focus on, i.e. the capabilities of the pre-initiative bio-firms' marketing and management teams and the quality and strength of their technology and finances, so as to improve their chances of forming alliances with sectoral investor actors (Department of Enterprise, Trade and Employment, 2008).

A key factor impinging on the bio-sector's development is the limited availability and restricted nature of sectoral investor actors. The public VC developments, introduced since 2001, were necessary to address the virtual absence of investor actor involvement in the pre-initiative sector, yet the lack of alternatives to these VCs has fed into the narrow focus of post-initiative commercial developments.

Essentially, the variety of available investor actor funding must expand. Bio-firms require different funds and investor skills at different stages of their development, i.e. there is a need for seed capital investors, and risk capital investors for new high-risk areas. Additionally, brokerage services, including business angels, are also required to optimise interactions between innovators and investors by building up reputation, trust, and perceptions of reliability among regional partners.

As the level of commercial activity in the bio-sector is too limited to facilitate such developments through private actor actions alone, they should be introduced through public sponsored measures which seek to advance firm-based developments to a degree where private investment actors emerge and/or enter the sector organically. As attracting private and/or non-Irish investors into the bio-sector ultimately depends on the successful post-initiative firm developments, this will be a long-term development target. It is vitally important that the bio-sector's investment actors and supports ultimately become private actor dominated so as to address its currently limited entrepreneurial nature/character, while the current public actor domination will become unfeasible as the bio-sector evolves.

In relation to 'soft' entrepreneurial supports, a key issue undermining sectoral entrepreneurial activities is a general absence of entrepreneurial and/or commercial skills throughout the bio-sector. Different options exist in how to address these issues.

Tailored education and training development programmes should be introduced to seed entrepreneurial skills across all areas of the bio-sector, so as to engender an entrepreneurial mindframe. Such programmes will require a long-term focus in order to fully address the ingrained/established nature of old and out-dated skill sets present in many sectoral actors. While new skills can be introduced through tailored programmes, ultimately a suitable entrepreneurial mindframe can only be engendered, and transmitted to future generations, through seeding the relevant competences, in combination with the long-term accumulation of acquired experiences and tacit knowledge exchanges, which accumulate over time through sectoral activities, this issue relates to sections 8.3.3 and 8.3.4.

In particular, such programmes should seek to address the existing 'divide' between academics and commercial actors. The level of commercialisation experience/knowledge among PREO academics and administrators is a key issue

inhibiting the bio-sector's optimal development. Furthermore, the commercialisation elements of education programmes in the PREOs are relatively minor, at best comprising small portions of the overall course content in under- and post-graduate courses. This means future academic and bio-firm actors enter their professional careers with minimal commercial experience and knowledge.

Addressing these issues will require a major recasting of the traditional ethos of Irish PREOs and their administrative structures, so as to create the relevant attitudes, skills and procedures. These developments must also occur parallel to the introduction of suitable resources and funding supports so as to optimally support commercialisation efforts.

Seeding PREO commercialisation skills should optimally occur through an evolving skills development initiative that seeks to engender the relevant competences and skills from the start of an academic's education and career, i.e. at the under-graduate level, and deepen them as students/academics work their way through the PREO system. Through introducing more advanced and structured commercialisation elements to education programmes, which optimally should include industrial placements (detailed further below), the commercial orientation of students would become more pronounced through making them more aware of the commercial possibilities in their future careers.

In relation to academics, comprehensive educational programmes should be introduced to educate academics on the commercialisation procedures of the PREOs, the roles of the relevant government agencies, and available funding sources. It must be noted that various commercialisation programmes have been developed by the quality promotion and professional development offices of the different PREOs, and are run in conjunction with their commercialisation offices. However, these programmes have been developed and implemented largely without government agency involvement/consultation, i.e. they do not form part of a coordinated commercialisation skills development drive, and no uniformity exists among them. Overall, they have had limited success, as reflected in the limited commercial developments generated by PREO actors, particularly in the context of the on-going commercialisation support developments.

Commercialisation education programmes for academics could be developed and implemented through a public/private mentor programme that identifies suitable

academic candidates and tailors programmes to optimise their skills development by covering all areas relevant to commercialisation processes. These developments could also link into, and complement the more pronounced commercialisation focus of the 'new' non-local academics, i.e. those attracted to Ireland through SFI's TFF, and actors returning to academia from industry positions, thus engendering spillover developments.

A key element of such efforts must be the development of industrial placement programmes for academics, and also PREO-based placements for industrial actors. Placements are essentially untapped elements in the bio-sector with regards to exposing academics to the practises and demands of commercial actors, and in facilitating more complex downstream networks and spillover developments.

However, the lack of established structures among both PREOs and bio-firms to facilitate such placements and to deal with the associated administrative and resource issues must be addressed. Such structures could be developed in association with the introduction of non-local skills and resources. In relation to bio-firm placements, they should be implemented as part of the on-going government initiatives, e.g. they should be introduced as required elements in publicly funded spin-out bio-firm developments, and in any future funding initiatives targeted towards developing PREO/bio-firm alliances. However, the success of such a programme would be dependant on the overall level of research conducted by indigenous bio-firms increasing.

The level of commercialisation and entrepreneurial skills present among indigenous bio-firms, even in the context of the on-going initiatives, remains limited. To a large degree this is due to the general absence of an established entrepreneurial mindframe in Ireland, as stated in the Culliton Report (1992), due to the relative absence of an innovative indigenous industrial base. This has inhibited the development of a culture which accepts even minor acceptance of trial and error through entrepreneurial experimentation, and is compounded by the absence of inter-actor networks.

Additionally, entrepreneurial experimentation in the bio-sector, and among SMEs in the wider economy, is undermined by the limited availability of skilled business development and management actors. This impacts on the ability of both pre- and post-initiative bio-firms to access speculative investor finance. Yet, the limited innovation

activities of the bio-firms further restricts their ability to access business management skills, i.e. a negative feedback loop exists.

Optimally, such missing commercial and entrepreneurial skills and competences should be identified and addressed through coordinated long-term skills development programmes derived through a public/private actor dialogue process, e.g. through exploiting the connections established by the BioConnect organisations and sectoral placement programmes. This would require seeding the relevant competences and the presence of suitable and evolving entrepreneurial supports, in order to engender the conditions which facilitate the organic build up and development of a particular/unique set of competences in the wider economy, specifically through entrepreneurial experimentation in innovative developments over an extended period of time.

The infrastructural suggestions presented in this section are presented to the Departments of Finance, the DETI, and EI. These management skill proposals are directed to the DETI.

8.3.3 An inter-actor network development programme

The international bio-sector is characterised by its inter-actor network structure; the sector's value chain is inherently network-based, and is rooted in tacit and codified knowledge spillovers, particularly in relation to 'sticky' knowledge exchanges embedded in localised social interactions. Networks are crucial elements in developing a bio-sector's internal logic, through facilitating and encouraging spillovers and entrepreneurial developments.

The indigenous bio-sector's network structure is disjointed, limited, and, in the case of many actors, networks exist predominantly with non-Irish actors. In part, this scenario is due to the limited numbers of sectoral actors and the resultant limitations in sectoral activities, yet it is also due to inter-actor networks not being intrinsic elements of current Irish industrial policy measures (Enterprise Strategy Group, 2004).

An effective methodology for such an Irish-based networking programme, developed upon the Danish Government's Network Cooperation Programme, has already been developed in an Irish setting. Forbairt ran a Pilot Programme on Inter-Firm Co-operation Networks between 1996 and 1997, and successfully established inter-actor network developments. Yet, despite the programme's evaluation report recommending

that a full-scale national programme be developed, no further action was subsequently taken.

This programme should now be reanimated, up-dated and tailored through the public/private actor dialogue process to the demands and needs of the indigenous bio-sector, and also to strengthen collaborative alliances where they exist. Due to the central role of trust in how networks develop and function, and in the context of the current state of the bio-sector's network 'structure', such a network development programme would require a long-term approach.

Yet, there is a clear need for a deeper understanding of the concept of inter-actor networks among development agencies. To address this issue, a programme development advisor could be used to re-introduce, and educate public actors on the concept and the associated benefits of inter-actor networks, through providing key insight into linkages and interdependencies between actors in supply chains in order to seed the concept and to better inform policy formation.

Overall, a network development programme would assist in engendering a more innovative bio-sector through addressing the poor levels of inter-actor collaborations. It would also facilitate significant sectoral feedback events, particularly the circulation of filtered PREO and firm-based knowledge of research activities, management practises, and would also feed into and optimise the public/private dialogue process.

This policy suggestion is directed towards EI, the DETI, and the DES.

8.3.4 Market information exchange resources

The current level of inter-actor information exchanges in the bio-sector is limited due to the lack of established interactive and collaborative infrastructures or dialogue processes which facilitate cross-system information dissemination. In part, this is due to the absence of established public/private actor dialogue systems and defined centralist Government structures in the wider economy. These issues limit sectoral synergies and spillover developments, and undermine the bio-sector's development trajectory. For such an information dependent sector as biotechnology, this limitation must be addressed through the development of cross-system discussion forums and information disseminating systems.

Such developments would require the establishment of infrastructures and resources to allow the gathering, filtering and dissemination of information. Such structures should link in with the proposed PREO and entrepreneurial services and infrastructures and inter-actor network development approach. Business and competitive intelligence services require extensive business know-how and local contacts to suitably service the bio-sector's needs, while the sectoral strength and confidence derived from self-regulation through inter-actor networks are also required for such an interactive service to work optimally (Anderson et al., 2004; Malecki, 1997; Engel and Del-Palacio, 2011).

The initial development of such a support/service would require public actor leadership in the context of the bio-sector's current state of development, while a limited level of indigenous bio-firms means substantial downstream contacts cannot be developed. Currently, such a service falls somewhere between the actions/roles of the IDA Ireland and EI, yet should also involve the Irish BioIndustry Association, BioConnect Ireland and its off shoots, and InterTradeIreland in a coordinated system that builds upon and advances existing national, cross boarder and international networks to facilitate resource and skills exchanges.

The development of cross-system discussion forums could also link in with the proposed public/private dialogue process. As it often takes several years until policy effects can be fully detected, in order to allow all sectoral stakeholders to have a broad view of all topics relating to the bio-sector, it is important to consider the implementation of continuous benchmarking, technology assessment and technology foresight exercise processes to inform the formulation and implementation of tailored sectoral development initiatives (Engel and Del-Palacio, 2011).

Additionally, such forums could facilitate the introduction of sectoral skills development programmes, in particular the introduction of non-local research and entrepreneurial skills developments. The skills base in the bio-sector must be subject to an on-going development processes to address the evolving needs of the bio-sector's actors, and to allow sectoral actors access up-to-date, relevant and different forms of skills and knowledge.

The development of international dissemination systems, i.e. placement programmes in more asset rich bio-sectors, and the formation of advice councils which draw from more

advanced and/or emerging systems, would allow sectoral actors to plug existing skills gaps, as identified through the public/private dialogue process, access new/emerging skills sets, and seed alternative skills and knowledge sets in the bio-sector. In the long-term, such programmes could potentially facilitate the attraction of non-local actors into the bio-sector and the development of a sectoral brand, however these developments would require a significant increase in the overall level of current sectoral activities.

Allied to these developments, it is crucial that PREO-based incubators and research parks are also developed to create key information exchange nodes between PREOs and industry actors. These developments must feed into the development of more advanced commercialisation supports and commercialisation skills programmes.

A very limited number of incubator developments (innovation centres) exist. Yet, incubators should optimally be developed at all PREO actors, including the IoTs and hospital RIs, and should link in with the EIBD-related developments proposed above. The business development skills of the existing (and future) incubators must also be expanded and re-enforced to provide a suitable commercialisation environment that facilitates and encourages researchers to develop commerciable IP and/or establish commercial alliances.

It is crucial that more advanced assessment procedures be introduced to ensure that the programmes which enter the incubators are of a suitable quality, so as to optimise commercial developments. A project's potential, and its specific criteria/needs must also be evaluated annually to optimise its development/realisation, and to remove underperforming firms/ideas. Such developments could be engendered through the cross sectoral discussion forums proposed above, i.e. through using a panel of visiting external experts to analyse and select a stronger selection of projects, optimise incubator programmes.

In relation to potential research parks developments, they should be introduced in the context of the various suggestions presented in the previous sections, and located at key PREOs, not at 'Green Field' sites, so as to facilitate increased localised commercial developments and knowledge spillovers among sectoral actors. However, their development would require that the level of sectoral activities, and the commercialisation skills, resources, capabilities and orientations of all sectoral actors

advance significantly beyond their current levels.

The suggestions presented in this section are directed towards the DETI, in respect of the agencies under its aegis

8.3.5 Actor and institutional density, and skill, competence and resource depth

A limited mass of entrepreneurial and innovative activity has formed in the indigenous bio-sector due to the existing weaknesses in the sector's PREOs, the limited level of downstream sectoral developments, and the absence of key market and non-market actors, institutions, and skills, competences and resources. As such, the bio-sector presently experiences difficulties in developing agglomerated economies, labour pools, skills, supply firms and other opportunities critical mass engender due to these systemic limitations.

To address these issues, and coordinate the bio-sector's development initiatives and development trajectory, an 'anchor' actor strategy could be developed to proactively engender a more pronounced private actor orientation to the bio-sector's activities, as its dominant actor is currently the National Government.

There are three anchor actor models:

- the organic development of a 'star' actor (e.g. a star bio-firm development);
- the organisation of systemic developments around the facilities of local TNC operations, and;
- an interdependent model where a mutually beneficial alliance develops between a system's actors and TNC operations.

Optimally, the development of a 'star', or anchor bio-firm would create an entrepreneurial role model in the bio-sector that could initiate an increased level of PREO spin-off developments by inculcating an entrepreneurial attitude/climate and driving the development of an entrepreneurial support system. Such an actor does not presently exist in the sector, or has yet to emerge.

However, anchor actor developments could be sought in alternative, niche areas in associated sectors indirectly related to the indigenous bio-sector, i.e. by facilitating PREO links with biotechnology-related small to medium sized enterprises (SMEs). It

must be noted that SMEs are identified here as separate entities to bio-firms, i.e. they were not formed solely to pursue the commercial development of basic or applied biotechnology research, but were formed by entrepreneurs that identified niche opportunities in sectors indirectly related to, and not centred upon biotechnology.

Forfás (1999) noted that a variety of established biotechnology-related sectors exist in the economy, i.e. the agriculture, marine, forestry, chemicals, food and drink, and environmental management sectors. While limited biotechnology-related research occurs in these areas, e.g. agriculture-related research activities are predominantly confined to Teagasc's RIs (Appendix E), they mean that significant latent potential exists in developing a more complex and varied indigenous bio-sector (Morrissey, 2011; Marine Biotechnology Ireland, 2011).

This proposal relates to the international bio-sector focusing mainly on pharmaceutical-based research and activities, specifically cancer- and drug/therapy-related areas. The Irish bio-sector has also developed a strong pharmaceutical orientated science base in the PREOs, while the majority of bio-firm activity is also related to pharmaceuticals. Essentially, the Irish bio-sector is focusing on competing in an already crowded/highly competitive market place.

This focus is not addressing or exploiting the massive range of opportunities and possibilities which biotechnology offers, or which Post-Fordism offers. Commercial applications of modern biotechnology have been most successful in specialist niche markets where economically competitive alternatives do not exist. Potentially, SME-based developments in biotechnology-related sectors represent a significant and essentially untapped and unexploited opportunity for Ireland to secure different forms of competitive advantage, as corresponding and underlying PREO-based research activities occur in a variety of alternative sectoral areas, e.g. marine, aquatic, and agriculture (Morrissey, 2011; Marine Biotechnology Ireland, 2011).

Such developments could expand the number of potential downstream alliances available to PREO actors, particularly for the more application based IoTs, and could lead to the development of a more research-orientated SME sector in areas related to biotechnology, which itself could feed into the development of a more diverse/multi-faceted bio-sector (STIAC, 1995; National Economic and Social Council, 1997).

The Irish industrial base is characterised as being engaged in very limited R&D activities, which restricts opportunities to develop research-based alliances with PREOs. Yet, a model for facilitating innovative SME developments, through alliances with PREOs, exists in the form of the Atlantic University Alliance (AUA). The AUA was established in 1999, through funding received from the National Development Plan 2000-2006, the EU, and its host universities, the University College Cork, UL and the National University of Ireland, Galway. The AUA proactively seeks to cultivate a more research-orientated SME sector through advertising relevant research programmes, and facilitate research-based collaborations with their partner PREOs. The AUA also allows interested/suitable SMEs to access PREO-based research findings and specialist academic advice so as to address technological issues they face. The AUA's commercialisation structure complements and supports existing structures in the 'parent' universities, i.e. the three universities work together, yet are independent of each other.
The AUA could be used as a template for the development of regional organisations to develop a more research-orientated SME sector in areas related to biotechnology, and to engender the concept of indigenous firms conducting R&D. This would require such a structure being developed nationally, and the introduction of a complex series of initiatives and supports similar to those proposed for the bio-sector in section 8.3.2 to address the limited innovative capacities of SMEs, and allow them develop the necessary capabilities and resources to absorb and apply research and new knowledge to their activities. Such developments would follow recommendations made by various Government publications relating to the development of networks and information sharing among indigenous firms.

SME-based developments could also be driven by alterations to existing Government regulations and procurement policies in order to create innovative pressures that drive biotechnology derived product developments. For example, the Environmental Protection Agency's Science, Technology, Research & Innovation for the Environment programme could be used to develop biotechnology-derived solutions to environmental issues, rather than just basic products or services (Forfás, 2006).

In relation to a TNC-centred anchor strategy, several issues make such a strategy essentially unsuitable for the indigenous bio-sector. An increased number of research-orientated TNC operations have been introduced into the country due to the proactive encouragement and support from the IDA Ireland. The current operational structures

and activity focus of the Irish-based TNC branch plants limit opportunities for significant sectoral alliances, while the limited state of the bio-sector's development would mean a TNC anchor strategy would essentially swamp the bio-sector's development trajectory, as their more advanced activities and resources would siphon off skills, resources and competences.

However, it is important that efforts to attract more R&D intensive TNC operations into the country continue, so as to facilitate more complex alliances with sectoral actors. Optimally, this would occur organically through sectoral activities attracting such developments into the country, yet current development trends indicate such development will not occur immediately. More complex TNC operations could be attracted through a series of inter-related policy measures, that link into the suggested initiatives presented above, as four distinct opportunities, which are concentrated around the country's PREOs, exist in the indigenous bio-sector.

Firstly, advanced drug incubator facilities are increasingly crucial to TNC as their research activities become more sophisticated. Drug incubators are specialised biopharmaceutical drug development laboratories where TNCs establish a drug master file, essentially a development template/blueprint that establishes result reproducibility and which informs the clinical trials process and later scale up processes. Such a file is vitally important in licence developments, and the demand for these facilities is greater then the global supply.

Academic respondents noted that by investing in such facilities, which are relatively cheap, Ireland could tap into a significant lucrative market. Suitable royalty-style agreements could generate considerable financial return for PREOs, as the value of such a small-to-medium scale production run is very high for TNCs. This strategy could attract more complex TNC R&D operations into Ireland, by advertising the depth and quality of Irish researcher skills, and PREO facilities and research activities, yet at a minimum would result in TNCs establishing more complex activities in the country.

Secondly, as part of their diversification strategies, TNCs are increasingly seeking to acquire IP from, or enter into licensing agreements with RIs. Academic respondents commented that this development presents Ireland with an opportunity to develop RIs specifically tailored towards TNC's research activities, so as to engender more complex

and engrained TNC research activities. Due to their defined TNC focus, such RIs would be separate to, yet compliment the structures of the current Centres for Science, Engineering & Technology. Such developments would be attractive to TNCs as they are increasingly seeking to address the rising costs of the clinical trials process. By developing alliances with such RIs, they would be able to conduct relevant research without the associated levels of capital investments. To a degree, this suggestion replicates the ready built factories offered by the IDA Ireland to entice FDI into Ireland.

Thirdly, PREO-based research parks could be developed which could link into the proposed commercial development services and supports and placement programmes for academics and students, so as to facilitate skills developments and engender spillovers. Such developments have occurred in the international bio-sector, e.g. Singapore's bio-sector, and would essentially mimic the IDA Ireland's existing TNC enticement strategy of providing pre-building factory space, yet in a more complex and advanced manner.

Finally, an opportunity exists for the bio-sector's public and private stakeholders, including the PREOs and downstream sectoral actors, to jointly formulate and implement tailored PREO education curricula that optimally address the bio-sector's various skill demands. This public/private stakeholder aspect is important to address information gaps in the development of such courses. TNCs could be allowed to inform the formulation of PREO education courses in order to address existing skilled labour shortages they are experiencing in several key areas of their operations. As international trends indicate that biotechnology will become increasingly important for TNCs, tailoring courses to the evolving demands and needs of TNCs would position the bio-sector to optimally address and adapt these trends.

The suggestions presented in this section are directed towards the agencies under the aegis of the DETI, the Department of Agriculture and Food, the Department of the Environment, Heritage and Local Government, and the Department of Finance, as well as City and Council Enterprise Boards.

8.5 CONCLUSION

Despite the various developments engendered by the on-going sectoral initiatives, the initiatives have failed to fully address the restricted innovative resource and skill capacities present in the bio-sector, particularly among PREO actors and pre-initiative

bio-firms, as well as the virtual absence of key value chain actors, e.g. TNCs.

In the context of the sectoral template and the regional systemic concentrations evident in the international bio-sector, as presented in chapter 3, these issues demonstrate that a more complex overarching policy framework, constructed through a public/private dialogue process, is required to engender a regionally tailored systems-based entrepreneurial and innovative support ecosystem which facilitates and drives entrepreneurial and innovative activities throughout the bio-sector's value chain.

The development of a suitable knowledge base, including the promotion of high-level basic and applied research, and skilled human resources must continue as a key policy focus. The country's PREOs should be remodelled to have a more overtly/defined commercial emphasis through introducing skills development services which seek to engender an entrepreneurial mindframe, so as to optimise the commercialisation of viable research. Such developments should feed into the development of improved commercialisation and entrepreneurial supports for downstream sectoral actors, particularly so as to optimise the development of existing and new bio-firms.

Additionally, a defined network development programme must be introduced, in alliance with structural supports, to facilitate increased inter-actor knowledge exchanges throughout the entire bio-sector, to optimise sectoral spillover developments, and the identification and exploitation of commercial opportunities in the bio-sector. Such developments should link into PREO-based structural and commercialisation-based resource developments in order to feed into new and on-going commercial developments.

The indigenous bio-sector's development trajectory could be orientated around an anchor actor strategy. Different options exist, yet optimally the bio-sector's development should be driven by indigenous commercial developments. Such an actor strategy may originate from the indigenous bio-sector, yet the wide reaching nature of the science of biotechnology means several sectors in the indigenous economy, in areas where potential biotechnology-derived applications may apply and/or be derived, could emerge as alternative anchor actors, thus facilitating the development of a more diverse and complex indigenous bio-sector.

CHAPTER 9:
A COMPARATIVE ANALYSIS BETWEEN THE IRISH AND INTERNATIONAL BIOTECHNOLOGY SECTORS

9.1 INTRODUCTION

This chapter is divided into two sections. The first section analyses sectoral actor, network, cluster/agglomeration and policy typologies in the international and Irish biotechnology sectors (bio-sectors). In particular, this section applies our understanding of these four elements, as derived from the Irish bio-sector analysis chapters, to the international bio-sector. This informs the second and final section, which presents a discussion on what this analysis demonstrates in relation to non-hub bio-sectors. This discussion seeks to highlight the importance of non-hub sector studies in advancing our understanding of the international bio-sector, specifically with regards to how sectoral development initiatives are formulated, structured and implemented in these bio-sectors.

9.2 ANALYSIS OF THE INTERNATIONAL CASE STUDIES AND THE IRISH BIO-SECTOR

Five hub biotechnology sectors/biotechnology clusters can be identified in the international biotechnology sector (bio-sector), three in the United States (San Francisco, Boston, and San Diego), and two in the European Union (Cambridge and Munich). These hub sectors/biotechnology clusters (bio-clusters) are the most studied sites in the international bio-sector; indeed the templates of sectoral actors, networks, bio-clusters and sectoral development initiatives presented in chapter 3, i.e. the foundations upon which the review of the Irish bio-sector was constructed, were derived from these bio-sectors.

In comparison to these hub bio-sectors, investigative studies on the actors, networks, regional agglomeration tendencies, and/or policy initiative forms of the remaining bio-sectors, i.e. the non-hub/Proto bio-cluster (PBC) sectors, are less intensive or comprehensive. In part, this is due to academic research focusing on the hub sectors in efforts to derive solutions to identified issues/weaknesses in non-hubs.

This means that little academic work has been done on how non-hub sectors can contribute to our understanding of the hubs, and the international bio-sector as a whole. Analysing non-hub sectors advances our understanding of the workings of bio-sectors by informing a more comprehensive understanding of how actors, networks, agglomerations/clusters and policy interact/function internationally in the context of

different pre-conditions, sectoral characteristics, and regulatory environments.

9.2.1 An analysis of the actor typologies of the international case studies and the Irish bio-sector

All sectoral actor types are crucial to a bio-sector's performance and activities, by acting as either an incubator or transfer mechanism within the complex and interactive Post-Fordist sectoral value chain, as presented in Table 9.1. Superficial analyses of hub bio-sectors can highlight specific actor types as being more important than others in sectoral innovation processes, yet such analyses ignore/miss many crucial relationships and inter-dependencies (Owen-Smith and Powell, 2007; Romanelli and Feldman, 2007).

Table 9.1: The main contributions of the international bio-sector's actor analysis to the Irish bio-sector
Commercial developments, internationally, are predominantly based upon the research programmes of Public Research and Education Organisations (PREOs). Their long-term speculative/exploratory basic research programmes and information transmission and information disclosure characteristics are important for volatile technology fields/sectors, e.g. biotechnology. The quality of their infrastructures and skills are vital in determining the depth and range of their research and skills development programmes.
Bio-firms traditionally occupy the middle rung in the sectoral innovation process, and are the main transferring mechanism of PREO-based research findings to the market place. Predominantly established by commercially minded PREO actors to pursue research that exhibiting clear commercial promise, they emerge in the context of significant commercial supports and competences that seek to optimise their development trajectories.
Bio-firm developments are dependent on formal alliances with different investor actors, particularly Venture Capital (VC) investors. VCs target high-risk businesses that traditional business investors avoid, and are key facilitators in firm developments by providing crucial managerial and technical expertise to optimise their start-up and initial developments so as to enter formal alliances with downstream actors, e.g. Transnational Corporations (TNCs).
TNCs are traditionally the last element in sector value chains, which includes the clinical trial process, and are increasingly adopting biotechnology in their operations as biotechnology research is easily adaptable to their technological requirements.
Government actors play critical roles in sectoral developments and activities through determining the depth/quality of hard and soft infrastructures, skills and competences of sectoral actors. This reflects the wide technological base and range of activities of biotechnology, which means that the direct and indirect involvement of Government departments and agencies in a bio-sector covers a wide remit.
Supply actors facilitate research and production activities throughout a bio-sector. Goods suppliers provide equipment, chemicals and biologicals bio-firms require for research activities, while service firms provide a wide range of advanced and specialised systems and solutions to issues that arise in different fields of biotechnology research. Sub-national centres disseminate region-specific information among sectoral actors, while trade associations circulate information and provide services relating to their members' core activities. Such actors can facilitate the development of sectoral brands which attract non-local skills and resources into a sector, facilitating positive externalities which deepen the hub nature of these bio-sectors.
Bio-firms in the hub sectors are increasingly focused on niche areas on inter-firm alliances. This has been facilitated by the emergence of specialist service provider firms which focus on specialist technological and research support services, i.e. platform technology firms (which provide specialist tools) and product development firms (which conduct specific aspects of the clinical trials process). In response, TNCs have restructured their operations to mimic the organisational structures of bio-firms and focus on smaller volume niche market drugs. These developments have fragmented the downstream end of the value chain of hub sectors, highlighting their actor, resource, and skills depth and variety and exposing the shortcomings and weaknesses of the non-hubs.

(Smith and Powell, 2004; Barley et al, 1992; Breschi et al., 1999; Prevezer and Tang, 2007; Avnimelech and Teubal, 2007; Gertler and Levitte, 2005; Stuart et al., 2007; Giesecke, 2000; Malecki, 1997; Forfás, 1999; Lia and Gengb, 2012).

Where a country's PREOs experience long-term absences of public actor investments, their research-related capabilities and activities will be restricted and undermined due to the presence of significant infrastructural, resource, skills and competence weaknesses. Such issues will be emphasised where structural rigidities and established institutional conservatism are present. Where such elements exist in the context of a general absence of commercial orientation among PREOs, they will undermine and strongly limit activities and commercial developments throughout a bio-sector's value chain, and will particularly undermine bio-firm-related developments and activities.

Substantial PREO-based infrastructural and skills developments can be engendered through the introduction of public actor initiatives which seek to address preceding

weaknesses and to ultimately drive sectoral activity levels by facilitating more advanced commercial developments. Yet, while introducing more advanced infrastructures and skill sets will result in noticeable advances, these developments will only create a development surge, i.e. the developments will be substantial in relation to the previously limited conditions and activities, yet they will not fully address the established path dependence of PREO actors.

Due to the restricted activities and capabilities of a bio-sector's PREOs, limited transfers to commercial concerns will occur. In such a scenario, where bio-firms do emerge, it will be common for bio-firms to source their Intellectual Property (IP) from non-local sources so as to bypass the weaknesses of the indigenous PREOs.

Such bio-firms will be characterised as being conservative in nature, i.e. the type/character of their activities will typically be in diagnostic- and platform-related activities. This conservatism will impact on the overall level of commercial activity of a bio-sector, and will contribute to the development of a sectoral innovation paradox, i.e. actors in poorly endowed regions do not/cannot engage in significant innovative activities as they typically under invest in Research and Development (R&D), which means they cannot/do not engage in significant R&D activities (Asheim and Isaksen, 2002; Anderson et al, 2004; Giesecke, 2000; Morris, 2011).

These conservative characteristics will be amplified if such bio-firms develop in the context of a virtual absence of commercial development supports, particularly an absence of investor actors, and their associated skills and competences. Such issues will further engrain and entrench a conservative mindframe among a bio-sector's actors, and will mean that bio-firms will seek alliances with investors in non-local sectors, specifically hub bio-sectors. Yet, due to the limited sectoral track record in entrepreneurial and innovative developments, and the costs associated with the management of such alliances over long distances, non-local investors are less inclined to enter into such alliances. This scenario will result in an investment paradox emerging, i.e. bio-firms cannot attract significant investor interest due to their limited developments, which exist due to their inability to develop significant commercial developments (Leydesdorff at al., 2002; Casper, 2002; Kaiser, 2002).

These paradoxes and the entrenched institutional and activity conservatism and

limitations will inhibit and constrict entrepreneurial and innovative activities throughout a sectoral value chain, i.e. extensive cumulative disadvantages will be experienced. As such, the bio-sector will fall further behind in relation to more resource endowed bio-sectors (Morris, 2011).

Where public actors seek to drive entrepreneurial developments in a bio-sector by introducing advanced commercialisation supports and infrastructures, in order to exploit the increased commercial potential derived from preceding PREO-centred initiatives, they will engender a surge in bio-firm developments. Essentially, more substantial bio-firm developments will emerge in the context of the preceding development levels, and will advance the commercial orientation of a bio-sector, yet the new bio-firm developments will hit significant structural weaknesses caused by the preceding conservative and limited sectoral activity levels of the bio-sector. Additionally, those bio-firms which emerged prior to the introduction of sectoral development initiatives will typically be excluded from the development initiatives, meaning their conservative natures and associated paradoxes will remain. This results in the formation of a disjointed bio-sector, which undermines and compromises the bio-sector's development trajectory.

Furthermore, public commercialisation supports can also undermine the bio-sector's development trajectory. Due to their public nature, investor actors will adopt a conservative nature as they seek to establish themselves in an unproven bio-sector, and also seek to successfully deliver noticeable returns for their substantial public investments. As such, conservative business models and activities will be sought, e.g. platform-related activities. This activity orientation feeds into and engrains the conservative nature of the bio-sector, and restricts entrepreneurial developments, rather than assisting them. Additionally, such supports will focus only on post-initiative bio-firms, thus contributing to the disjointed nature of the bio-sector.

Where the bio-sector's innovative development levels are restricted by PREO and bio-firm limitations, TNC involvement will be minimal as the limited collaborative opportunities will be available to them. This scenario is amplified where TNCs are predominately branch plant in nature, i.e. they have limited autonomy in their activities.

Even where a bio-sector undergoes a surge in sectoral activity as a direct result of public

actor development initiatives, TNC involvement will remain minimal as entrenched sectoral weaknesses mean activity levels will not advance rapidly to such a level where collaborations are possible. This scenario will remain even where increasing numbers of research operations are introduced by the TNCs into their branch plant operations, in a reflection of the increasing adoption of biotechnology practices in their operations, internationally.

Limited sectoral activities will undermine the development of sectoral support actors. As such, the main markets for the supply actors which do emerge in the context of limited indigenous sectoral activities will be in non-local bio-sectors, as they seek to bypass indigenous sectoral weaknesses. This will reinforce the adoption of conservative structures, and encourage the development of alliances with non-local suppliers among sectoral actors. Sectoral surges which result due to sectoral development initiatives will not change or address this situation due to the entrenched weaknesses of the existing pre-initiative bio-firms and the limited developments engendered by the post-initiative bio-firms.

The characteristics and activities of sectoral actors reflect the policy environment in which they emerge and develop. Where such an environment is shaped by long-term protectionist policies, and a subsequent pronounced focus on Foreign Direct Investment (FDI) driven industrial and economic developments at the expense of defined and pronounced indigenous industrial development initiatives, a country's indigenous industrial base will be strongly compromised by the limited entrepreneurial and/or innovative developments such policy approaches will engender. Indeed, these approaches will facilitate the emergence of an innovation paradox in the wider industrial base. This scenario will be amplified where there is long-term uncoordination between public industrial and STI policy streams. Furthermore, where policy formulation and implementation occurs through a top down process that has virtually no regional elements, differences in regional development trajectories will become established and engrained due to different regional endowments of sectoral actors and activity levels, which can cause imbalanced regional development and thus undermine the development of a national bio-sector.

Where a Government identifies biotechnology as being a key strategic target in securing the future development of its economy, development initiatives are typically formulated and derived from 'snapshots' of the hub bio-sectors, i.e. they focus superficially on

elements of the substantial infrastructures, skills, and resources which characterise the hub bio-sectors, in efforts to mimic their depth and range of sectoral activities. Due to the manner in which they are formulated, the ultimate impact of snapshot-derived initiatives will be limited as they will not/cannot address the substantial and long-term cumulative weaknesses found among a bio-sector's actors and value chain. Indeed, such an approach can even contribute and entrench sectoral weaknesses.

Snapshot public initiatives will be unintentionally introduced in an uncoordinated staged manner, due to the manner in which they are formulated. Typically, the public initiatives will initially focus on developing the infrastructures and capabilities of the country's PREOs. These elements are viewed as automatically facilitating the emergence of substantial commercial developments, and are seen as being sufficient to achieve this aim. Yet, while such initiatives can lead to rapid developments, relative to the conditions and activity levels which existed prior to their introduction, it will subsequently become apparent that further initiative developments are required to address various competence issues and structural bottlenecks that inhibit commercial developments, e.g. the general absence of entrepreneurial skills, competences and supports among sectoral actors.

Commercialisation development supports will subsequently be introduced, particularly dedicated VCs funds so as to facilitate commercial developments. Yet, due to their public nature, they will fail to address engrained weaknesses which undermine commercial developments, and they can also entrench entrepreneurial conservatism through seeking and supporting conservative business models in efforts to optimise their investment returns. Additionally, these initiatives will not seek to, or be able to address the limited involvement of TNCs and supply actors.

9.2.2 An analysis of the network typologies of the international case studies and the Irish bio-sector

The international bio-sector's value chain is a complex, non-sequential network-based Post-Fordist structure. The knowledge base from which biotechnology innovations draws is embedded in formal and informal networks between various actor types, including public and industrial researchers, while the development of biotechnology-derived products and processes involves many different formal and informal actor alliances at various stages of a product's and/or process's development. Informal and formal networks are important for all aspects of sectoral activities, as detailed in Table

9.2. Informal networks are crucial in innovative developments, while formal networks are important for crucial transfers of codified knowledge and play central roles in commercial developments. Inter-actor networks are optimised where close relationships and spatial proximity exist between actors.

Table 9.2: The main contributions of the analysis of the international bio-sector's network structure to the Irish bio-sector
The sectoral innovation process can be characterised as a tripartite alliance chain formed around the coordinated efforts of PREOs, bio-firms, and TNCs, who create a non-linear, continuously interactive structure in which a hierarchy cannot typically form. Their interactions act as feedback loops that update and alter innovation processes for the benefit of all network members. Sectoral network structures are place specific, reflecting actor activities, historical factors (accumulations of infrastructures, resources, skills, and competences), and evolving policy environments.
Academic scientists engage in collaborative basic research programmes that involve filtered tacit knowledge and information exchanges, and codified scientific and technical competence exchanges. Their programmes can be characterised as space specific agglomerations of scientific knowledge, where regional endowment of researchers and resources determine the effectiveness of networks in localised learning processes.
Codification of PREO research occurs through journal publications and patent development/licensing agreements with commercial actors. Yet, a pronounced entrepreneurial orientation among academics may lead to the creation of bio-firms so as to exploit commercially viable research. Entrepreneurship is an inherently localised phenomenon, determined by place specific developments of skills, competences and experiences, and the presence of entrepreneurial-related policy actions.
Alliances between bio-firms and PREOs represent the first downstream stage of the biotechnology innovation process. Bio-firms seek to locate close to their 'parent' PREO(s) to maintain/engender knowledge exchanges and skill transfers through informal and formal networks. Relative geographic proximity and social inclusiveness determines how they maintain/engender relationships with academics so as to access their 'filtered' tacit and codified knowledge. Such alliances determine a firm's research capabilities, and influence its commercialisation activities. Bio-firms can also derive their organisational structures and internal practices from their parent PREO(s).
Alliances between bio-firms and other commercial actors, particularly TNCs, represent the second stage of the biotechnology innovation process. This represents the downstream end of the sectoral value chain, inter-actor networks become predominantly formal in nature (TNC/bio-firm alliances are facilitated through formal strategic networks with investor actors, particularly VCs). TNCs seek alliances to exploit the IP of bio-firms, offering the firms their extensive resources and infrastructures, while the firms offer their advanced research activities and capabilities.
Suppliers play facilitator roles in sectoral activities, forming close formal and informal networks with sectoral actors. These relationships are increasingly important as sectoral technologies and processes are increasingly niche orientated. Indeed, exclusive supply alliances can form, driving sectoral network structure depth and density. Sub-national and trade associations are key information disseminating services, and can facilitate sectoral brand development that attracts in non-local actors and boosts sectoral depth and density.
Governments indirectly and directly facilitate sectoral network developments in many ways. The dominant organisational practices and routines of actors can be indirectly influenced by Government actor actions (e.g. the structures of PREOs influence the structures adopted by bio-firms). The development of intermediary actors, e.g. incubators and science parks, can facilitate network developments between PREOs and commercial actors. Governments can also develop or guide network promotion programmes.
Hub sector network structures are increasingly complex due to the niche orientation of bio-firms and the downstream value chain fragmentation, i.e. the niche research/activity focus of bio-firms means inter-firm alliances are more equitable than alliances with TNCs, while TNCs have restructured their research operations to mimic the organisational structures of bio-firms and established virtually independent research operations that mimic bio-firm locational patterns to engender alliances with PREOs.
Dense agglomerations of bio-sectoral activity develop in the hub sectors as non-local actors seek to locate in these sectors so as to develop alliances with the advanced activities of their PREOs and bio-firms. These developments will drive and engrain the development trajectory of these hub bio-sectors, which means they will experience cumulative advantages. These developments demonstrate inter-actor networks are increasingly crucial in the internal activities and logic of sectoral actors and activities, and emphasises the impact network structure weaknesses in non-hubs have on their entrepreneurial and innovative activities.

(Morgan and Nauwelaers, 1999a; Owen-Smith and Powell, 2007; Erden and von Krogh, 2011; Gertler and Levitte, 2005; Gilding, 2008; Giesecke, 2000).

Non-hub bio-sectors are essentially little more than combinations of co-locating actors, principally bio-firms and PREOs, grounded in regional ambitions to become significant players in the global bio-sector. Their network structures are poorly developed due to the presence of extensive structural inflexibilities, e.g. limited innovation levels caused by regional specific limitations in the resources, skills and competences of their actors, and the presence of various paradoxes, including innovation and investment paradoxes, which undermine and inhibit sectoral activities and developments. As such, their value chains are fragmented, and their sectoral activities are compromised.

Where a bio-sector's PREOs are poorly developed, limited transfers will occur among academic researchers, which will undermine innovative developments, or to commercial actors, specifically bio-firms. The absence of alliances with commercial actors will become engrained due to the absence of an entrepreneurial mindframe, resources and

competences among academics and administrators. To compensate, a common strategy for non-hub bio-firms is to develop distant collaborative network strategies with actors located in more knowledge and resource rich bio-sectors. This issue is demonstrated by the prevalence of the pre-initiative bio-firms sourcing their IP from non-local sources.

The limited and conservative nature of bio-firms is compounded where there is a general absence of sectoral supports, particularly VCs. Due to such weaknesses, bio-firms will adopt conservative business models and activities. As such, these actors face significant issues in establishing alliances with non-local actors due to the poor image/reputation of the indigenous bio-sectors and the intense competition they face from more dynamic bio-sectors. This scenario will also undermine sectoral network development opportunities as they cannot/will not develop significant alliances with PREOs or with other commercial actors, e.g. TNCs, due to their conservative activities. This issue is amplified where TNC operations in the wider economy are manufacturing branch plant in orientation.

Public initiatives can be developed in efforts to address many of these issues, e.g. PREO-based infrastructural and skills developments can be sought to facilitate significant increases in intra- and inter-institutional exchanges of personnel, competences and resources. Inter-actor sectoral networks can indeed surge as a result of such initiatives, and may superficially resemble networking patterns found in the hub bio-sectors, e.g. the advanced research activities in the post-initiative research institutes and their close proximity to their 'parent' university have facilitated significant spillover developments, and have impacted on the bio-sector value chain by facilitating an increased level of commercial activities and developments, i.e. the post-initiative bio-firm developments in the Irish bio-sector.

However, where such initiatives are introduced in a top-down manner and have no explicit/defined network elements, established and entrenched institutional and actor characteristics will mean limited intra- or inter-institutional collaborations will occur. Such a scenario can develop as the interactive nature of the sectoral value chain is often ignored and/or misunderstood, i.e. Government agencies can seek to develop inter-actor collaborations, not as part of a defined collaborative networking programme, but through using funding to essentially force actors to collaborate, predominantly so as to facilitate more optimal and efficient uses of personnel and resources. As such alliances

are not trust-based, they typically end once a project ends due to their contractual nature.

As a result, the deeply ingrained institutional inertia, and the virtual absence of an existing interactive mind frame/culture in a bio-sector, will not be addressed. Such issues will feedback through the sectoral value chain, meaning that new bio-firms will emerge into a compromised value chain which presents few opportunities for downstream collaborations. This means that the bio-sector's network structure will remain characterised by groupings of conservatively structured actors which engender limited spillovers, while alliances will continue to be sought with non-local actors as they continue to seek to by-pass on-going shortcomings of the indigenous bio-sector.

9.2.3 An analysis of agglomerations in the bio-cluster case studies and the Irish bio-sector

Hub bio-sectors form dense geographic concentrations of actors, partly due to the importance of spatially sticky tacit knowledge transfers between PREO and commercial actors through informal networks. These dense network structures are spatially concentrated in what are identified as bio-clusters.

Only five locations in the international bio-sector have developed bio-clusters to date, i.e. San Francisco, Boston, San Diego, Cambridge and Munich. Each bio-cluster underwent its own unique development trajectory and trigger process, indeed the presence of proto bio-clusters/non-hub bio-sectors in countries with bio-clusters emphasises the distinct spatial specificity of the issues which underline bio-cluster developments. However, commonalities can be identified in the elements which facilitate a bio-cluster's emergence, as detailed in Table 9.3.

Outside of the bio-clusters, similar features and elements can be identified in non-hubs, which can be termed proto bio-clusters (PBCs). For place specific reasons, they fail to develop a critical mass of entrepreneurial developments, and/or a suitable interactive system which drives and facilitates entrepreneurial developments. As such, negative spillovers occur which undermine their trigger processes and development trajectories. The PBCs are lagging behind due to their disjointed and suboptimal entrepreneurial and innovative infrastructures, resources and capabilities, and their compromised development trajectories.

Table 9.3: The main contributions of the international bio-sector's bio-cluster analysis to the Irish bio-sector
The bio-clusters emerged in the context of similar positive pre-conditions and seeds, e.g. established PREOs and the presence of related industries, e.g. TNCs. The bio-clusters emerged through the development of place specific trigger processes, i.e. complex processes which build upon and prime a bio-sector's substantial and positive pre-conditions and seeds and engender positive systemic path dependence and development trajectory.
Positive systemic path dependence and development trajectory facilitated the formation of a critical mass of entrepreneurial and innovative activity, i.e. a bio-cluster's trigger event, which emerges over an extended period of time and depends on the form, nature and character of a system's entrepreneurial and innovative support ecosystem and case specific information spillovers. There are three identifiable trigger event forms in the international bio-clusters: • the San Francisco and Boston bio-clusters emerged due to spontaneous trigger events, where the critical mass formed through private actor developments in an absence of public policy interventions, • the San Diego and Cambridge bio-clusters emerged through hybrid trigger events, i.e. their systems emerge through private actor developments, yet the trigger event was sparked by direct/indirect public actor initiatives, and • the Munich bio-cluster emerged due to a planned trigger event, where the system's trigger process and event was overwhelmingly driven by public actor initiatives. The character of a bio-cluster's trigger event determines the nature of its structure, the entrepreneurial and innovative features of its constituent actors, and a bio-cluster's typical business structure. This is reflected in the EU bio-clusters, which are more entrepreneurially conservative then the US bio-clusters due to the planned nature of element of their trigger processes, while their system structures are characterised as having limited inter-actor networks and systemic spillover events due to the continuing impacts of their limited pre-conditions and existing systemic path dependences.
Following a bio-cluster's emergence, its sustainability, in relation to how it extends and consolidates its competitive advantage(s), is determined by how it is subject to a continual, structured and self-reinforcing process of growth and development through on-going innovative and entrepreneurial activities. The case specific nature of bio-cluster systems means a limited number of themes can be derived from the bio-cluster case studies, i.e. second generation (spin-off) firm developments (particularly evident in the San Francisco bio-cluster) and an influx of non-local actors, in particular TNCs and VCs.
The bio-clusters are driving sectoral developments and activities in the internal bio-sector due to their intense private actor dominated entrepreneurial and innovative systems. Essentially, the bio-clusters are advancing rapidly, relative to the remainder of the international bio-sector, due to the magnetism, deep entrepreneurial capabilities and low entry barriers of their systems.

(Chiaroni, and Chiesa, 2006; Romanelli and Feldman's, 2007; Feldman and Braunerhjelm, 2007; Wolfe and Gertler, 2007; Bresnahan et al, 2001; Engel and Del-Palacio, 2011)

Where a bio-sector experiences long-term cumulative infrastructural and actor weaknesses, its compromised path dependence and development trajectory will result in a fragmented and restricted value chain. Essentially, these issues mean that a suitable collaborative environment, i.e. an established networked sectoral structure, cannot and will not develop. In combination, these issues mean that the conditions required to facilitate the development of a systemic trigger process will not form, as entrepreneurial/innovative and spillover developments will be undermined by negative systemic developments.

Such issues will be strongly determined by the policy environment in which a bio-sector emerges and develops. Where a Government formulates its policies without private actor involvement, and implements its initiatives in a top down manner, its policies will be reactive in nature and they can fail to address (and may even entrench) sectoral issues through being poorly designed and/or unsuitable for sectoral activities. This issue can be demonstrated by the presence of disjointed industrial and STI policy streams and the presence of an innovation paradox in the wider industrial base, while an interactive environment which facilitates systemic developments will not form where inter-actor networks or interactive structures are not defined elements of public initiatives.

Additionally, where a country's Government is centralist in structure, i.e. where Government structures do not have implicit/defined regional structures, differences in

regional development trajectories will be ignored. This creates and engrains regional imbalances in how a national bio-sector develops, i.e. locations with relatively more complex endowments of infrastructures, skills and resources will experience more substantial spillover developments and will advance at a greater rate relative to less endowed regions. This will undermine a national bio-sector's development trajectory, as the less endowed regions will experience cumulative disadvantages as the more advanced regions will draw away skills and resources from them.

9.2.4 An analysis of the policy themes of the international case studies and the Irish bio-sector

There are an enormous range of policy forms and approaches in the international bio-sector due to different Government structures and case specific historical issues. For ease of presentation purposes, Table 9.4 discusses generalised policy themes that are observable in the hub/bio-cluster case studies.

Where a bio-sector emerges and develops in the context of a policy environment that is shaped by disjointed policy themes, the legacy of long-term protectionist policies, and a pronounced (and on-going) FDI-centred orientation to industrial development policies, its development trajectory will be restricted by the resultant limitations and conservative natures of its actor types, their limited entrepreneurial and innovative activities, and the disjointed and limited nature of the sectoral value chain these features engender.

Where Governments introduce development initiatives to advance the activities of their indigenous bio-sectors, these initiatives will typically be developed from snapshots of leading international bio-sectors, i.e. they are derived from observable positive aspects of hub bio-sectors/bio-clusters. Policies derived from 'snap shots' of hub bio-sectors are poorly developed as they ignore important elements and features of their case study bio-sector(s) and of their indigenous bio-sectors. Such initiatives typically result in the adoption of top down policies that seek to engender large scale developments, e.g. advanced sector wide commercial developments solely through PREO-centred investments. This ultimately and unintentionally results in the staged introduction of uncoordinated initiatives over a series of stages (over an extended period of time) that focus on addressing specific big issue topics. They typically have clearly defined timeframes and funding amounts, and will focus on engendering 'quick' results, so as to justify the sometimes substantial investments made by these initiatives.

Table 9.4: Review of the international bio-sector's policy themes
The US bio-sector emerged in the context of substantial Federal Government investments, particularly the Cold War era PREO funding initiatives, which did not focus on a particular sector, but on the wider economy and industrial base. They seeded extensive positive factor conditions and created the advanced entrepreneurial support ecosystem which subsequently exploited the commercial promise the PREO investments engendered. The entrepreneurial supports were also introduced to facilitate developments in the wider economy, and indirectly seeded a defined entrepreneurial/innovative culture which subsequently facilitated and optimised the US bio-sector's development trajectory following its emergence in the mid-1970s. A complex set of predominantly private actor driven, mutually reinforcing and aligned interests emerged, in the context of these indirect and aligned public interests and supports, which fostered the development of their value chains and enabled their trigger processes to engender a critical mass of entrepreneurial activity. Public policy measures in the bio-cluster, following their emergence, continue to focus on the wider industrial base. They are adaptive, responsive and attuned to the demands and needs of local actors through constant upgrading and development through advanced and evolving public/private actor dialogue processes at all Governance levels.
While similar features can be observed in the EU hubs/bio-clusters to those in the US bio-clusters, their trigger processes developed in the contexts of different Government structures: • The UK's National Government introduced indirect policy initiatives in the 1960s that engendered a national PREO-orientated entrepreneurial environment. This facilitated the emergence of pharma-TNC and NICT/electronics agglomerations in the Cambridge area, in combination with the area's established PREOs, which the sector subsequently slotted into. By the late 1980s, the area had begun to develop a mass of entrepreneurial/innovative activity, yet this was constricted by investor actor limitations. • In Germany, prior to the emergence of its bio-sector, significant Federal and Land investments facilitated the development of an advanced PREO base, while an established TNC sector had also emerged. However, the German policy environment was not focused on engendering a similar pro-entrepreneurial environment as found in the US and the UK, e.g. defined structural rigidities between university and research institute actors undermined collaborative activities, while contractual restrictions inhibited alliances between PREO-based and commercial actors. In combination with the dominance of the indigenous TNCs, and the relative absence of a commercialisation culture or support infrastructures, minor entrepreneurial/innovative activities had occurred in the German bio-sector by the mid-1990s. Due to European Union driven efforts to encourage its member states to address the rising dominance of the US bio-sector in the mid-1990s, extensive policy initiatives were introduced throughout the EU to engender more advanced sectoral developments and activities. Both EU clusters emerged as a result of these actions. The Cambridge sector experienced a hybrid trigger event as the Department of Trade and Industry implemented various biotechnology initiatives to improve the competitiveness of the wider UK industry base through promoting biotechnology processes and practices in non-biotechnology sectors, while the Munich bio-sector experienced a planned trigger event through the extensive supports/infrastructures introduced by the Federal Government's BioRegio programme. The governance structures in the EU bio-clusters remain hierarchical/public actor dominated, and are disjointed in comparison to the US bio-sector's policy environment.
The US bio-sector is the basis on which many of the policy forms and approaches of the non-hub bio-sectors are derived from due to the observable 'hard' and 'soft' strengths of its bio-clusters, e.g. productivity advantages through specialised components and/or services inputs, collective marketing activities, intense innovative pressures due to geographic proximity between suppliers and customers, and business and innovation advantages created by the presence of multiple suppliers and institutions.
The Munich bio-sector and the BioRegio programme, which was derived through an analysis of the US sector, have become the international templates for Governments designing comprehensive bio-cluster development programmes. The programme demonstrates that cluster specific policies must be substantial in shape and form in order to link in with existing preconditions and seeds, and to create an ecosystem that focuses on facilitating and driving entrepreneurial developments. Essentially, cluster specific policies must be co-ordinated, large scale, and adaptive and reactive in nature, through private actor involvement, so as to optimise their formulation, development and implementation. The ultimate aim of such policies must be on the long-term development and building up of seeds and preconditions, and addressing existing infrastructural, resource, skills and competence issues through cumulative positive spillover/externalities.
The presence of PBCs in countries which have developed bio-clusters demonstrates that place specific issue play a central role in bio-cluster development and emergence.

(Giesecke, 2000; Romanelli and Feldman's, 2007; Feldman and Braunerhjelm, 2007; Wolfe and Gertler, 2007; Engel and Del-Palacio, 2011)

Initially, such initiatives will focus on advancing the infrastructures and resources of PREOs in the anticipation/expectation that they will automatically drive sectoral developments by generating commercially viable research. Yet, limited innovative and commercial developments will ultimately emerge due to the absence of an entrepreneurial mindframe/culture in the PREOs and the limited availability of commercialisation supports. Subsequent initiatives will again be snapshot derived, and will seek to address limitations in sectoral commercialisation support infrastructures and resources, such as the absence of VC actors, in order to facilitate the emergence of commercial concerns. Yet, again, limited commercial developments will occur as the initiatives will not address entrenched structural or competence weaknesses.

While such policies will seed positives, e.g. advanced infrastructures, and facilitate sectoral surges in entrepreneurial and innovative activities, significant sectoral developments will not materialise as the initiatives fail to fully account for and surmount existing structural weaknesses and/or sectoral actor path dependence issues. Indeed, such staged initiatives will result in a suboptimal sectoral development

trajectory and can contribute to structural weaknesses.

These issues demonstrate that seeking to develop an innovative industrial sector which is characterised by a complex Post-Fordist interactive structure, through snapshot-derived initiatives, where an indigenous bio-sector is characterised as being entrepreneurially conservative and structurally fragmented, is problematic for a variety of reasons.

Where sectoral actors are seen as being unique entities, not as active participants in an inherently interlinked value chain, development initiatives will fail to address the presence of a poor interactive environment, the absence of crucial collaborative skills and competences, and the presence of innovation and/or investment paradoxes. Furthermore, where such initiatives are formulated with limited private actor involvement and implemented in a top down manner, they will fail to address intricate and complex systemic weaknesses which can be embedded in the institutional characteristics of a bio-sector's actors through imposing impracticable and/or unsuitable initiatives.

These issues demonstrate that where a country seeks to develop an internationally competitive bio-sector, in the context of the substantial cumulative strengths of hub bio-sectors/bio-clusters and the distinct policy environments that characterise them, sectoral development initiatives need to be take the form of a comprehensive, long term co-ordinated framework environment which addresses the inter-linked and inter-dependent elements of their sectoral innovation processes as a whole.

Such an approach requires public actors to fully understand what they are seeking to develop, i.e. they must fully understand the exact needs requirements and demands of a bio-sector, how it is structured, how it functions, as well as the exact needs of its actors. This means that private actor involvement at the local level is required at all stages of initiative formulation and implementation. Failure to develop such an approach will mean that systemic/structural weaknesses will not be surmounted, due to poorly designed/unsuitable initiatives, and that sectoral development efforts will flounder.

Initiatives must focus on creating the conditions which facilitate and drive entrepreneurship and innovative developments throughout a bio-sector's value chain. As

such, a multi-element approach must be adopted which creates the necessary infrastructures, skills and competences to facilitate such developments. As stated, these initiatives must be informed and shaped by public/private dialogue processes and implemented in a manner which acknowledges and addresses regional differences in sectoral activity and development trajectories. Essentially, it is the process by which bio-sectors form and emerge, not the final 'result', which is important in relation to policy initiatives. This means that public actors should seek to become sectoral facilitators, not constructors, in the long-term, i.e. that private actors eventually direct and guide sectoral developments (Anderson et al., 2004; Martin and Sunley, 2001).

9.3 DISCUSSION

The international bio-sector case studies demonstrate that the vast majority of available academic and public actor literature on the international sector focuses on the hub sectors/bio-clusters. This focus reflects their more advanced activity levels and states of development, and also reflects the common use of these studies in determining what are perceived as being the optimal way/manner in which to advance the development of non-hub bio-sectors.

Such studies typically focus on specific aspects of the value chains of the hub sectors, e.g. a specific relationship type, such as PREO/bio-firm relationships, and/or on specific policy approaches. As such, they can be characterised as being 'snapshot' analyses of aspects of sectoral structures and activities, i.e. they do not fully account for a bio-sector's entire value chain, its actors or their characteristics, its on-going path dependence/development trajectory, its interactive nature, or its policy environment at different Governance levels.

This delimited approach is questionable for two reasons. Firstly, as such studies selectively analyse elements or sections of a hub bio-sector, their findings can therefore be misinterpreted and/or skewed by being taken out of their proper context(s). Secondly, non-hub sectors share few common elements/features with hub bio-sectors, making the effectiveness of such comparisons ultimately questionable.

The pronounced focus on hub bio-sectors reflects the little academic work which has been done on how non-hub bio-sectors can feed into our understanding of the hub bio-sectors and the international bio-sector as a whole. Yet, the analysis of the Irish bio-

sector, presented in chapters 5, 6, 7 and 8, demonstrates that analysing a non-hub sector in depth substantially contributes to and adds to the general understanding of the key concepts in the international bio-sector, and also shows that non-hub bio-sectors must be analysed on their own place specific terms, not only/solely in the context of hub sectors. Essentially, this analysis demonstrates that an opportunity exists to develop an area of economic geography that is specifically centred on non-hub sectors/PBCs. The principles underpinning this proposition are discussed below.

The actor typology study of the Irish bio-sector demonstrates that while the value chain of hub sectors can be characterised as a tripartite relationship between PREOs, bio-firms and TNCs (with VCs, Government actors, and supply actors playing key facilitator roles), a hierarchy of specific actor types can be identified in non-hub sectors. Specific actors play more central roles in such value chains, i.e. RIs are the main PREO actor type, innovative developments are essentially confined to new bio-firm developments, while public VCs play key facilitator roles in entrepreneurial developments.

The case study also shows that specific actors play relatively peripheral roles in non-hubs, i.e. university- and research hospital-based research programmes are not key sources of commercial sectoral developments, regional associations and supply actors play limited roles due to limited sectoral activity levels, while the participation of TNC research elements occurs mainly through distant networking strategies. Furthermore, the Irish case study demonstrates the need for place specific approaches to sector actor analyses, as the Institutes of Technology do not appear in the PREO actor typologies presented in chapter 3

However, the most important sectoral actor-related issue that the Irish study emphasises is that Government agencies and departments are typically *the* central/dominant actor type in non-hub sectors. Government agencies and departments seek to engender sectoral developments through introducing various initiatives (this is discussed further below), and their dominance reflects the extensive and engrained nature of private sector actor weaknesses and the disjointed manner of non-hub value chains.

The Irish study also emphasises how the place specific nature of a non-hub sector's actors determines the nature and character of its formal and informal inter-actor networks and influences its entrepreneurial and innovative developments. As stated

above, non-hub sectors are essentially little more than combinations of co-locating actors that are grounded in regional ambitions to become significant players in the global bio-sector. Structural weaknesses, caused by place specific resource, skill and competence limitations of key value chain actors, inhibit crucial information transfers and innovative developments, even where significant sectoral advances occur. The specific nature of such issues demonstrates that in-depth analyses of the interactive structural characters of non-hub sectors must occur, so as to properly identify sector specific causes and impacts of structural weaknesses throughout a value chain.

The Irish study shows that the formulation and implementation of public actor policy initiatives seeking to drive and facilitate non-hub sectoral developments must occur through an evolving and tailored process that addresses the place specific form, nature, and structures of a particular bio-sector. Using other sectors as templates or bench marks in formulating development initiatives is unrealistic, for several reasons. Aside from the selective nature of such studies making direct comparisons between hubs and non-hubs ineffective, as detailed above, 'snapshot' studies also set unrealistic development standards, i.e. non-hub sectors share only certain characteristics or features of hub sector actors, networks, development trajectories and/or innovative and entrepreneurial natures. Furthermore, deriving initiatives through studying bio-sectors which have emerged through planned initiatives is also problematic, as such sectors have developed through actions derived from hub sectors. Essentially this approach would entail a 'snapshot' analysis being derived from a 'snapshot' analysis, making such an approach particularly unsuitable.

While 'snapshot' derived policies can seed sectoral strengths, e.g. they facilitate relatively more advanced PREO-based activities and firm developments, such initiatives only succeed in engendering disjointed and staggered developments as they fail to address pre-existing and entrenched structural and competence weaknesses which undermine entrepreneurial and innovative developments throughout a sectoral value chain, e.g. the limited involvement of TNCs in sectoral activities and the lack of an entrepreneurial culture among indigenous actors.

The Irish study demonstrates that where a non-hub sector's government seeks to engender significant sectoral developments, a contextual, pluralist, and heterogeneous approach is required, one which is responsive, adaptable, and fine tuned to the needs,

demands and requirement of a sector's actors. Initiatives should seek to facilitate the emergence of a proactive and private actor driven entrepreneurial support infrastructure, and an entrepreneurial mindframe and culture in the sectoral value chain. As stated, entrepreneurship is an inherently localised phenomenon, and a system's propensity towards entrepreneurship is determined by past experiences and existing skills, competences and experiences.

It is imperative that initiatives are developed in the context of a complete understanding of the place specific nature of a non-hub sector's actors, the structure and interactive nature of its value chain, and the spatial differences in sectoral development trajectories, at local and national levels. Essentially, initiatives must focus on building upon local strengths and addressing local weaknesses through a long-term, localised, systemic approach that is formulated through a public/private dialogue.

Efforts to develop a non-hub bio-sector should focus on developing tailored entrepreneurial and innovative functional resource (EIFR) requirements (as detailed in chapter 3) that seek to facilitate and drive entrepreneurial/innovative developments along a sector's value chain over an extended period of time. An initial policy framework should be established through using the SWOT analysis tables presented in chapter 2. Essentially, initiatives should seek the development of place specific hard and soft infrastructures, resources, supports, skills and competences to form a tailored industrial environment that is adaptable and responsive to new entrepreneurial and innovative developments throughout a bio-sector's value chain. Successive long-term developments should be sought that engender positive feedback developments throughout a bio-sectors value chain, in order to optimise a bio-sector's development trajectory (Casper, 2007; Orsenigo, 2007; Rausser et al., 2000).

The Irish study demonstrates that a hierarchy can be identified among the EIFRs as they apply to non-hubs, i.e. knowledge infrastructure, resources and skills (EIFR 1), entrepreneurial infrastructure, resources and skills (EIFR 2), and inter-actor networks (EIFR 3) are crucial requirements in facilitating and driving sectoral entrepreneurial and innovative developments. EIFR 2 is particularly important, as entrepreneurship is the main issue which determines the long-term success of a sector through facilitating spillover developments. Market information exchange resources (EIFR 4) should develop alongside the other EIFRs, yet it depends on a positive development trajectory

emerging, while such a development will ultimately feed into and drive actor and institutional density, and skill, competence and resource depth (EIFR 5).

The study also demonstrates that non-hub sectors should seek to focus on developing place specific forms of competitive advantage. Internationally, non-hub sectors are focusing on competing in pharma-biotechnology related developments, which has resulted in the formation of a global mass of diagnostic and platform technology firm developments. Aside from the capacity issues this development raises, significant questions must be asked as to the long-term effectiveness of this approach in the context of the extensive positive spillovers hub sectors engender through their advanced entrepreneurial and innovative systems, i.e. non-hub sectors will essentially remain peripheral and reactive to current and future developments in pharmaceutical biotechnology. The opportunities Post-Fordism and biotechnology present to non-hubs in creating competitive advantages in niche areas in bio-sectors and related sectors are not being addressed by non-hub sectors. Essentially, non-hub sectors should tailor their policy initiatives towards their local strengths to develop 'niche' areas in which they possess/can develop competitive advantage(s).

CHAPTER 10:
CONCLUSION

10.1 INTRODUCTION

Drawing from the theoretical framework of the thesis, this chapter synthesises the main material, under the main headings of sectoral actors, inter-actor networks, industrial clusters, and policy measures to facilitate their development, and also assesses what can be drawn from the interpretation of the material in light of the aims of the study. The chapter also discusses the contribution of this dissertation as a whole to the literature, and to efforts to optimise and facilitate the on-going development of the indigenous biotechnology sector (bio-sector).

This chapter is divided into three sections. The first section presents a general discussion on the main findings of the thesis. The second section discusses the implications of these findings and makes recommendations relating to on-going and future policy initiatives. Finally, the third section discusses the contribution of the thesis to the academic literature in economic geography.

10.2 SUMMARY OF THE MAIN FINDINGS OF THE THESIS

The modern international bio-sector emerged in the mid 1970s following the establishment of Genentech in the San Francisco Bay Area. Genentech's formation and its rapid development established a biotechnology firm (bio-firm) development 'template' that continues to shape the international bio-sector's main development pattern, i.e. the commercialisation of the explorative research programmes of Public Research and Education Organisations (PREOs) through the creation of a bio-firm, whose development is optimised through strategic alliances with a Venture Capital firm (VC), and which is floated on the stock market and/or enters into strategic alliances with a Transnational Corporation (TNC), so as to access the necessary knowledge sets and revenues required in bringing a product to the market place.

This template established the tripartite nature of the bio-sector's value chain between PREOs, bio-firms (the value chain linchpin), and downstream commercial actors, e.g. TNCs. These actors create a non-linear, continuously interactive structure in which a hierarchy cannot typically form. Their interactions, which are supported and facilitated by region-specific support structures, act as feedback loops that update and alter the sectoral innovation process, optimising the process for the benefit of all network members (Malecki, 1997; Morgan and Nauwelaers, 1999a; Owen-Smith and Powell,

2007).

The tripartite nature of the international bio-sector's value chain is an example of a complex network-based innovative high-tech Post-Fordist sector, i.e. the knowledge base from which biotechnology innovations draws upon is embedded in complex formal and informal networks between various actor types, including PREO and industrial actors, while the development of biotechnology-derived products and processes involves many different formal and informal actor alliances, which have different spatial patterns, that form at various stages of a product's and/or process's development.

Networks can be generally classified as being either formal or informal in nature. Formal networks are rigidly structured relationship agreements in which actors agree to collaborate to achieve a common business goal or goals, or more sophisticated business practices than they can/could achieve independently. Due to their rigidly structured, sometimes contractual nature, only the members of a network benefit from these alliances. Formal alliances involve codified knowledge and information exchanges, i.e. knowledge/information embodied in machinery and equipment, which is codified through documentation, manuals, patents and scientific papers (NESC, 1996; Owen-Smith and Powell, 2004; Pitt et al., 2006)

Informal networks are loosely structured social connections that primarily involve the diffusion and transfer of knowledge/information through face-to-face interactions between network members. They are heavily dependent on, and are regulated, by inter-actor trust and reciprocity as they involve the diffusion of tacit knowledge, i.e. privately held knowledge and expertise accumulated by technical and research personnel through practice and experience gained at the interface between organisations, and which is optimised where close geographic proximity and relational norms exist between network members (NESC, 1996; Malecki, 1997; Delaney, 1993; Gaya and Dousset, 2005).

The bio-sector's innovation process begins with PREO-based scientists engaging in collaborative and exploratory basic research programmes characterised by informal, strategic, exploratory, and exploitative networks that involve exchanges of filtered tacit and codified scientific and technical competences and research-related equipment and resources. Such networks develop through the under-graduate and post-graduate, and professional careers of academics, as well as through industrial and/or PREO work

placements and publications (Malecki, 1997; Owen-Smith and Powell, 2008; Prevezer and Swann, 1996).

PREO organisational structures and research capabilities depend on their place specific research communities and infrastructures, which represent idiosyncratic and localised knowledge fields of researcher specific tacit knowledge. As such, PREO-generated knowledge can be characterised as being spatially 'sticky', due to its predominantly tacit nature and being closely tied to the location in which it is generated (Powell 1996; Malecki, 1997; Owen-Smith and Powell, 2008; Gertler and Levitte, 2005; Prevezer and Swann, 1996).

PREOs proactively promote information transmission and dissemination through lecturing, publications, placements, and conference presentations. Research programme findings are ultimately codified through publications, or through a license developed by (a) commercially minded entrepreneurial academic scientist(s) that seeks to engender commercial developments, i.e. a patent development or start-up bio-firm development, where commercially viable Intellectual Property (IP) is generated (Casper and Murray, 2005; Malecki, 1997; Smith and Powell, 2004).

Where commercially minded academics seek to develop formal commercial alliances with commercial actors, i.e. bio-firms and TNCs, they seek to access the financial resources and technological capabilities of the commercial actors. These alliances also allow academics to gain insight into emerging industrial trends, needs and requirements (Casper and Murray, 2005; Smith and Powell, 2004; Giesecke, 2000; Lundberg and Andresen, 2012).

PREO/bio-firm alliances represent the first stage of the biotechnology innovation process, i.e. research enters the product development process. As bio-firms are predominantly founded by entrepreneurial academics, as stated, they will typically locate in close proximity to their 'parent' PREO(s). Close relations with PREOs determines a bio-firm's research capabilities by optimising informal and formal alliances through reducing transaction costs and insecurities by minimising the distance over which interaction and communication are conducted. These elements are important due to the increasingly niche orientated nature of bio-firms, internationally, and enhance inter-actor task coordination, codified resource and knowledge transactions, and

engender crucial knowledge spillovers (Balconi et al., 2004; Sorenson, 2003; NESC, 1996; Rowley et al., 2000; Uzzi, 1996).

Bio-firms also seek to develop close networks with PREOs to source skilled human capital, while transfers of organisational routines may occur through formal business competence exchanges during a bio-firm's initial set-up phase. This means they model their organisational routines and structures on those of their 'parent' PREO(s), which can facilitate increased network flows among the network members as the presence of common organisational forms means that structural similarities exist, i.e. mimetic isomorphism. Mimetic isomorphism facilitates organisational proximity and reduces perceptions of risk in alliances (Owen-Smith and Powell, 2008; Powell and Brantley, 1992; Romanelli and Feldman, 2007; Zhang and Haiyang, 2011).

Mimetic isomorphism can result in increased sectoral network density as, where actors face uncertainties, they model themselves on organisations they perceive as being successful. Those elements observed as being most efficient and effective are diffused, fine-tuned and replicated among network members, and gradually evolve into accepted routines and procedures that lead to a common vision, further advancing experimentation and adoption. This can place competitive pressure on similar actors in an area to do the same so as to improve their ability and suitability to form alliances, further engraining the non-reproducible, regional specific characteristics of a network's structure (Owen-Smith and Powell, 2007; Cooke, 2002; Slack and Hinings, 1994; Scott, 2007).

Alliances between bio-firms and downstream commercial actors, e.g. other bio-firms and TNCs, represent the second stage of the biotechnology innovation process, i.e. product development enters the clinical trials drug development process (Owen-Smith and Powell, 2007).

Bio-firms traditionally seek formal financial, resource and business knowledge networks with VC firms so as to access the necessary funding and business skills they require to optimise their development trajectories. Such alliances facilitate strategic developments and re-modelling of bio-firm management structures in order to allow VCs optimise their chosen exit strategy, i.e. a stock market floatation and/or strategic alliances with a TNC.

Alliances with TNCs represent the final stage in the sectoral value chain. Such alliances constitute research and business networks that facilitate exchanges of tacit and codified scientific and technological competences and resources. TNCs access the scientific capabilities of bio-firms, i.e. their ability to evaluate external scientific knowledge, and also their technical capabilities, i.e. its ability to utilise external knowledge. Bio-firms access the established marketing, supply, manufacturing, sales, and distribution networks of the TNCs (Malecki, 1997; Powell and Brantley, 1992).

The nature of downstream alliances in hub bio-sectors has stratified due to the increasingly niche orientated nature of bio-firm activities caused by the rising costs and durations of research programmes, due to increasing regulatory demands and commercial competition. As such, the relative size of bio-firms to TNCs have shrunk, making inter-firm alliances more equitable than those with TNCs. This has been facilitated by the establishment of bio-firm forms which focus on specialist technological and research support services, i.e. platform technology and product development firms. Additionally, second generation bio-firms have emerged, i.e. an established bio-firm spins-out a new bio-firm so as to continue (for example) a research programme which emerges within its existing activities but without stretching its finite resources (Powell and Brantley, 1992; Ernst and Young, 2001; McMillan et al., 2000; Giesecke, 2000).

TNCs have responded to these developments by increasingly adopting biotechnology practices into their product development activities, establishing their own biotechnology research laboratories, and/or reorganising their operations to mimic bio-firm structures and locational patterns. As such, two main elements to the network structures of the leading bio-sectors can be observed, i.e. 'traditional' vertical innovation networks, where bio-firms act as the main mechanism between PREOs and TNCs, and horizontal product development networks between different forms of bio-firms, i.e. drug discovery and service/platform technology firms, and TNCs (Gertler and Levitte, 2006; Giesecke, 2000; Owen-Smith and Powell, 2007).

Geography plays a key role in determining how the bio-sector's innovation process is replicated internationally. Two broad sectoral forms can be identified, i.e. hub and non-hub bio-sectors. These differences exist as regional endowments of actors, and their

ability to generate and assimilate locally- and externally-sourced knowledge, are not homogeneous. Furthermore, the non-structural underpinnings of the behavioural characteristics and social regulations of actors can also be region specific. As such, geography means that different regions have non-reproducible, regional specific organisational forms and targets that form a local knowledge community or organisational field, and which determines the innovative capabilities and development trajectory of a bio-sector (Owen-Smith and Powell, 2004; Ozman, 2006).

Non-hub sectors can be characterised as being little more than combinations of co-locating actors, principally bio-firms and PREOs, grounded in regional ambitions to become significant players in the global sector. Their network structures are poorly developed, and are characterised by limited innovation due to regional limitations in institutions, resources, and skills (Powell et al., 2002; Gertler and Levitte, 2005; Malecki, 1997).

In comparison, the network structures of the hub sectors, i.e. San Francisco, Boston, and San Diego, and (outside the US) Munich and Cambridge, act as collective entrepreneurs where actors form dense regional specific concentrations/critical masses of complex and varied forms of skills, resources, information and networks that facilitate rapid transfers of information/knowledge and resources to engender sector-wide innovative developments, and the development of self-supporting and generating regional agglomerations (Anderson et al., 2004; Feldman, 2001; Malecki, 1997).

The hub sectors form dense geographic concentrations of actors and network structures, partly due to the importance of tacit knowledge transfers between PREOs and commercial actors through informal networks, that can be identified as biotechnology clusters (bio-clusters). A bio-cluster can be conceived as a mode of organisation of a productive system that contributes to the innovation and competitiveness of its actors. The interdependencies/collaborative arrangements among actors are at the concept's centre. Bio-clusters are trust-based, voluntary, non-contractual systematic relationship arrangements that have no membership limits, in which actors collaborate and compete to facilitate acquisitions of wider competencies and to build competitive advantage in a local system of specialised sub-supply, service providers and institutes (Rosenfeld, 1997; Porter 1998; vom Hofe and Chen, 2006).

The industrial cluster concept was developed by Michael Porter (1990), through his analysis of the factors determining national competitiveness. Porter argued that individual nations gain competitive advantage in particular industrial sectors that portray strong tendencies to concentrate within particular regions. At a national level, Porter conceived clusters as broad industry groups linked within the overall macro economy, at the regional level, constituent elements share common regional locations, including urban areas, labour markets, or other functional economic units (Porter, 1998).

Porter focuses on the importance of close proximity in facilitating synergistic interactions between actors that generate innovations. Proximity stimulates innovation by facilitating knowledge and technology transfers through repeated trust-based exchanges, i.e. networks. Only through constant innovation and upgrading, including product and organisational methods innovation, can competitive advantage be attained and sustained.

Porter proposed four broad determinants of national competitive advantage, i.e. factor conditions, demand conditions, related and supporting industries, and firm strategy, structure and rivalry, which form a mutually reinforcing system where the effects and influence of one determinant is dependent on the state of the others. How they interact, and the influence of two additional factors, i.e. chance, and the role of Government, create the context, individually and as a system, in which firms are created and compete, and determines why particular locations develop bio-clusters, and others do not.

As stated, few locations have developed bio-clusters, which emerged in the context of similar positive pre-conditions and seeds, e.g. established PREOs and the presence of related industries. Yet, these elements alone cannot facilitate a bio-cluster's emergence. This occurs through a place specific trigger process, i.e. complex processes which build upon and prime a bio-sector's pre-conditions and seeds, and engenders positive systemic path dependence and development trajectories which facilitate the formation of a critical mass of entrepreneurial and innovative activity. This critical mass is a bio-cluster's trigger event, which emerges over an extended period of time, and depends on the form, nature and character of a system's entrepreneurial and innovative support ecosystem, and case specific information spillovers.

There are three identifiable trigger event forms in the international bio-clusters:

- the San Francisco and Boston bio-clusters emerged due to spontaneous trigger events, where critical mass formed though private actor developments, in an absence of policy interventions,
- the San Diego and Cambridge bio-clusters emerged through hybrid trigger events, i.e. their system's emerge through private actor developments, yet the trigger event was sparked by direct/indirect public initiatives, and
- the Munich bio-cluster emerged due to a planned trigger event, where the system's trigger process and event was overwhelmingly driven by public initiatives.

A trigger event's character determines the nature of a bio-cluster's structure, the entrepreneurial and innovative features of its constituent actors, and its business structure. A bio-cluster's trigger process reflects the policy environments within which it emerges.

Due to the visible success of the bio-clusters, governments and supra-national organisations have sought to engender similar developments in their own economies, through strategy approaches typically derived from the observable patterns, processes and institutional arrangements in the bio-clusters. As such, they can be characterised as being reactive in nature, as public actors are directly removed from industrial development trends, while their essentially top down nature can fail to address intricate and complex systemic weaknesses through imposing impracticable and/or unsuitable initiatives. This means that the envisaged entrepreneurial developments fail to emerge, meaning that the development trajectories of the PBCs remain compromised and fail to result in the formation of critical masses of entrepreneurial and innovative developments.

These issues can be identified in the Irish bio-sector. The Irish Government first identified biotechnology's importance for Ireland’s future development in the late 1970s, yet serious and sustained efforts to develop a significant indigenous bio-sector were not introduced until the late 1990s. Prior to the late 1990s, limited sectoral developments occurred due to inter-related issues along the sectoral value chain. A general absence of PREO activity occurred due to extremely limited infrastructural and skills investments by public actors. As such, limited transfers or spillover developments occurred where PREO-based actors sought to enter into or engender commercial developments. This was compounded by the relative absence of commercialisation skills and competences

among academic researchers and University administrators, and the limited and disjointed nature of commercialisation supports and infrastructures available to PREO actors.

These issues impacted on sectoral commercial activities prior to the late 1990s. The bio-firms which formed in this environment had very limited innovative capacities due to their inability to form substantial alliances with PREO actors, while the limited development supports, specifically dedicated VCs, meant they adopted conservative business models. As such, they had limited desire or capacity to enter into significant alliances with sectoral actors. It must be noted that opportunities to develop alliances with commercial actors were small due to the limited level of sectoral activity and the limited involvement of key actors, such as TNCs, in such activities. Overall, the bio-sector's network structure was compromised by a lack of innovative activity, poor skills, competences and resources and the limited/conservative nature of many sectoral actors.

These issues reflected national circumstances, particularly the various industrial and science, technology and innovation (STI) policies from the early 1920s onwards. Until the late 1950s, in the context of a protectionist policy environment, industrial policy focused predominantly on facilitating indigenous agriculture-related developments, while limited emphasis was placed on industrial or PREO-based developments. Furthermore, the industrial and STI policy strands were segmented. From the late 1950s onwards, more open economic measures were adopted as the emergence of high emigration rates and a balance of payments crisis undermined the protectionist approach. The industrial policy focus switched towards attracting foreign direct investment (FDI) branch plants into the country. Little emphasis continued to be placed on indigenous industrial developments, while the industrial and STI policy strand segmentation remained.

By the early 1980s, significant issues began to undermine the FDI development approach, particularly the emergence of 'jobless growth', i.e. TNC branch plants increased productivity through adopting more automated production methods, not through expanding their workforce. Several Government sponsored reports subsequently highlighted the on-going innovative limitations in the indigenous industry base, e.g. the 'Telesis Report' in 1982, and the 'Culliton Report' in 1993, and called for and proposed measures to address this issue. However, no serious attempts have been

made to address this issue in the wider economy. Essentially, the overwhelming thrust of industrial policies remains focused on attracting FDI activities into the economy.

However, the orientation of public industrial and STI policy altered in the late 1990s, when new information and communication technologies (NICTs) and biotechnology were identified as strategic technologies that would underpin existing and future sectors in the Irish economy. The Government introduced a series of development initiatives to enhance and ensure Ireland's future competitiveness in these areas. However, it must be noted that the Government's focus on facilitating the emergence of internationally competitive high-tech sectors was/is anomalous in the context of indigenous industrial development efforts in the wider economy.

Initially, the bio-sector initiatives focused on addressing the poor state of the country's PREO infrastructures and capabilities, with the ultimate aim of driving commercial developments throughout the sector. This focus engendered significant developments, in particular the introduction of advanced research institutes (RIs), yet failed to result in a significant increase in commercialisation due to the presence of significant structural weaknesses. Subsequently, more substantial commercialisation supports, in particular VC funds, were introduced to facilitate the emergence of more complex and innovative commercial developments from the advanced PREO activities. This resulted in a surge of commercial activity in the context of the pre-initiative sector's activity levels.

Yet, the on-going initiatives have not delivered the intended/expected level of sectoral developments, as numerous established structural issues have essentially created a PREO centred 'bubble' of sectoral activity, and restricted transfer of the advanced PREO-based activities into commercial developments. These issues include:

- significant weaknesses in the commercial orientation of PREO academics and administrators,
- limitations in the resources, skills and capabilities of the PREO-based technology transfer actors,
- on-going limitations in the commercialisation supports available to sector actors. Despite the introduction of dedicated VC funds, their relative age, size and public nature means commercial developments are and will remain limited in scale and scope. Additionally, they are conservative in nature as they are

unproven investors in an unproven bio-sector, and thus seek conservatively structured business developments,

- the limited nature of pre-initiative bio-firms not being targeted by, which means their ability to enter into sectoral alliances remains limited,
- the post-initiative bio-firm developments are 'new' in terms of their innovative intensity and the manner of their origin, yet due to the conservative nature of the entrepreneurial supports and the entrepreneurial environment they have emerged into, they mimic the pre-initiative bio-firms by adopting conservative business models. This inhibits possible/potential upstream and downstream alliances within the sector's value chain.
- the limited level of inter-actor networks among indigenous actors, and
- the continuing limited involvement of Irish-based TNC operations in sectoral developments, due to their branch plant nature.

These issues reflect the on-going segmented nature of the industry and STI policy strands, and the reactive and top down nature of the on-going initiatives, i.e. they are not attuned to the specifics of the indigenous bio-sector's value chain, and are not suitably addressing the long standing and complex nature of the interrelated sectoral weaknesses that inhibit and undermine commercial/entrepreneurial developments.

10.3 POLICY IMPLICATIONS AND RECOMMENDATIONS

In the context of the current state of the post-Celtic Tiger economy, efforts to engender the development of innovative indigenous industry are vital, as Ireland's continuing dependence on FDI is not conducive for the long-term development of a strong, vibrant and sustainable economy, even where increasingly high-tech intensive TNC elements are being attracted into the country. However, the current policies relating to innovative industrial developments in the bio-sector are not working optimally. The main issue undermining the sector’s development is the relative absence of entrepreneurial developments caused by the presence of inter-related structural weaknesses. These issues have not been addressed due to the uncoordinated manner of the on-going initiatives, and the top down manner in which they have been formulated and implemented.

Essentially, there is a pressing need for the introduction of an overarching framework so as to create a support ecosystem that facilitates and drives entrepreneurial and innovative activities throughout the sector's value chain. Optimally, such a development requires a long-term approach that transcends election and business cycles, and involves substantial

private actor input into their formulation and implementation so as to address information gaps and improve their accuracy.

The on-going PREO developments must continue as a key policy focus, yet more advanced initiatives must be introduced to promote high-quality basic and applied research so as to further advance skills developments, and to retain and attract skilled researchers into the sector. In order to optimise infrastructural and skills development efforts, the different PREO actors should be remodelled so as to form more integrated structures. A more defined commercialisation mindframe must also be indoctrinated among administrators and academics in order to optimise commercial developments from the PREOs. Commercialisation skills development services should be introduced, in collaboration with more advanced commercialisation and entrepreneurial sectoral supports, to optimise new bio-firm developments.

A key issue inhibiting the bio-sector’s development is the limited level of inter-actor networks in the indigenous value chain. The concept of networking has only entered the vernacular of Government agencies over the last 10 years, and despite the increased importance placed on the concept in Government publications, no defined network development programme has been introduced in any area of indigenous industry. A network development programme must be introduced, one that links into PREO-based structural and commercialisation-based resource developments, so as to facilitate increased inter-actor knowledge exchanges and to optimise sectoral spillover developments. This development would allow sectoral actors to better identify and exploit commercial opportunities which emerge in the sector, in combination with enhanced commercialisation supports.

A network programme should link in with the development of information exchange services to facilitate the circulation of sectoral information, and to facilitate more informed strategic decisions by sectoral actors. Such services could facilitate the development of a sectoral brand that coordinates sectoral developments and attracts in non-local skills, competences and resources.

The bio-sector's development could be orientated around an anchor actor. Different anchor strategy options exist, yet optimally the sector's development should be driven by indigenous commercial developments. While an anchor actor may originate from the

indigenous bio-sector, the wide reaching nature of the science of biotechnology means alternative anchor actors may be found in other areas of the indigenous economy where potential biotechnology-derived applications may be developed. The niche areas identified in chapter 8 represent a significant opportunity to expand the range of biotechnology applications in the indigenous industrial base, and would facilitate the development of a more complex bio-sector.

These ecosystem suggestions, individually or in combination, would require a shift in the current orientation of the Government's industrial policies, in particular the suggestion to focus on indigenous industrial innovative developments instead of FDI. An additional challenge for public actors would be the development of tailored regional initiatives to optimise the development of the three identifiable 'hub' locations in the indigenous bio-sector, as detailed in chapter 7, due to the established centralist structures of the Irish Government and the absence of defined regional aspects to Government policies or programmes. Spatial differences in accumulations and endowments of firms, institutions, and social capital exist, which mean that regional differences in development trajectories will continue.

Region specific and tailored systems-based initiatives might engender the conditions that ultimately facilitate bio-cluster emergence. Yet, while the possibility of bio-cluster emergence is essentially impossible to gauge, particularly in the context of the bio-sector's current state, focusing on engendering an entrepreneurial and innovative ecosystem will optimise the indigenous bio-sector's development trajectory, and may engender bio-cluster emergence by creating a diverse economic base that supports new markets and internal diversification, though only through a long-term development process.

10.4 CONTRIBUTION TO THE LITERATURE

This thesis represents an in depth study of the evolution and development of an emerging sector in the Irish economy, the indigenous bio-sector. The study presents an analysis of the nature and capabilities of the bio-sector's actors, the formal and informal inter-actor networking arrangements found in the sector's value chain, and the policy environment within which the bio-sector has developed.

These elements have been analysed through a review of the actor types, collaborative inter-actor network structures, and geographic locational trends found in international bio-sector case studies, i.e. hub sectors/bio-clusters and non-hub sectors/proto bio-

clusters. Additionally, the analysis reviewed the nature of the entrepreneurial and innovation support environment provided by public and private actors in these different bio-sectors, and the main policy measure themes which influence(d) their development.

The study found that the vast majority of academic and public actor literature on international sectors focuses on the hub sectors/bio-clusters. This reflects their more advanced activity levels and states of development, and also their common use in determining what are perceived as being the optimal way/manner in which to advance the development of non-hub bio-sectors. Typically, such studies analyse selective elements or sections of a hub bio-sector, and do not fully account for a bio-sector's actor characteristics, its on-going path dependence/development trajectory, its interactive nature, or its policy environment at different governance levels. This delimited approach is questionable, as their findings can be misinterpreted and/or skewed by being taken out of their proper context(s), while non-hub sectors share few common elements/features with hubs.

The pronounced focus on hub bio-sectors reflects the little academic work which has been done on how non-hub sectors contribute to our understanding of the hub bio-sectors and the international bio-sector as a whole. The analysis of the Irish bio-sector shows that non-hub sectors must be analysed on their own place specific terms, not only/solely in the context of hub sectors. Essentially, the analysis demonstrates that an opportunity exists to develop an area of economic geography that is specifically centred on non-hub sectors/PBCs. The principles underpinning this proposition are discussed below.

Space has a significant impact on how sectors form, function and develop. Place specific constructions of competencies, actors, supporting institutions, and organisational structures occur under idiosyncratic natural, cultural, social and economic conditions that are “shaped and constrained by past decisions, chance events, and accidents of history” (Wolfe and Gertler, 2007: 244), and which involve complex inter-actions of heterogeneous public and private actors (Orsenigo, 2007; Swann and Prevezer, 1998).

The Irish bio-sector actor typology study demonstrates that a hierarchy of actor types can be identified in non-hub sectors, i.e. RIs are the main PREO actor type, innovative

developments are essentially confined to post-initiative bio-firms, while public VCs play key facilitator roles in entrepreneurial developments. The largest role in non-hub sectoral activities is that of Government agencies and departments due to the presence of extensive and engrained private sector actor weaknesses, and the desire of the public actors to facilitate sectoral advances due to the strategic importance placed on biotechnology in the country's future economic performance.

The study also demonstrates that certain actors play relatively peripheral roles in non-hubs, e.g. university- and research hospital-based research programmes are not key sources of commercial sectoral developments, while the participation of TNC research elements occurs mainly through distant networking strategies. Furthermore, the presence of an actor type not found in the actor typologies presented in chapter 3, i.e. the Institutes of Technology, emphasises the need for place specific approaches to sector actor analyses.

The study emphasises the inherent role of inter-actor networks in the functioning of a bio-sector's value chain, and demonstrates how they are determined by place specific factors, including the prevailing nature of actor competences, skills and resources, and structural weaknesses which influence entrepreneurial and innovative developments, and inhibit network formations. The place specific nature of these issues demonstrates that in-depth analyses of the interactive structural characters of non-hub sectors must occur, so as to properly identify sector specific causes and impacts of structural weaknesses throughout a value chain.

The study adds to our understanding of the difficulties and issues non-hub bio-sectors face when attempting to establish themselves in a highly-competitive high-tech global industry, particularly where they operate in a small open economy characterised by limited indigenous industrial activities and a high dependence on inward investment from Transnational Corporations. Using other bio-sectors as templates or bench marks on which to develop policy sectoral development initiatives in non-hub sectors can seed sectoral strengths, yet such an approach ultimately fails to address pre-existing and entrenched structural and competence weaknesses which undermine entrepreneurial and innovative developments.

The study demonstrates that sectoral developments should optimally be engendered

through an evolving and tailored process that addresses the place specific form, nature, and structures of a particular bio-sector. The study provides a detailed series of policy suggestions for both the Irish government, and for governments in non-hub sectors elsewhere, in terms of the range and nature of measures that are required to optimally develop indigenous biotechnology industries, the approach with which such measures should optimally be formulated and applied, and the prospects for success of such measures.

The formulation and implementation of policy initiatives seeking to drive and facilitate sectoral developments should optimally occur through a contextual, pluralist, and heterogeneous approach. It is crucial that initiatives are developed in the context of a complete understanding of the place specific nature of a bio-sector's actors, the structure and interactive nature of its value chain, and the spatial differences in sectoral development trajectories, at local and national levels. This means a public/private dialogue process, which involves sectoral actors, is required to ensure a long-term, systemic approach to policy development and implementation is developed.

Initiatives should seek to facilitate the emergence of a private actor driven entrepreneurial support infrastructure, and an entrepreneurial mindframe and culture among the sectoral value chain. Ultimately, initiatives should seek the development of hard and soft infrastructures, resources, supports, skills and competences that form a tailored industrial environment that is adaptable and responsive to new entrepreneurial and innovative developments. Successive long-term developments should be sought that engender positive feedback developments throughout a bio-sector by building on local strengths and addressing local weaknesses through a systemic approach based upon entrepreneurial and innovative functional resource (EIFR) requirements.

The study demonstrates that a hierarchy can be identified among the EIFRs as they apply to non-hub bio-sectors. Three EIFRs, i.e. knowledge infrastructure, resources and skills (EIFR 1), entrepreneurial infrastructure, resources and skills (EIFR 2), and inter-actor networks (EIFR 3), are particularly important in establishing positive path dependence in a value chain. EIFR 1 determines the strength of the technological foundation on which sectoral developments occur. EIFRs 2 and 3 are crucial requirements in facilitating and driving sectoral entrepreneurial and innovative developments. EIFR 2 is particularly important, as entrepreneurship determines the

long-term success of a sector through facilitating spillover developments.

In contrast, market information exchange resources (EIFR 4) develop alongside the other EIFRs, yet ultimately depend on a positive development trajectory emerging. Such a development will ultimately contributes to and drive actor and institutional density, and skill, competence and resource depth (EIFR 5).

The ultimate development of dense agglomerations of sectoral activity, and the likelihood of bio-cluster emergence, depend on the engenderment of a positive place specific trigger process and the cumulative development of actor and institutional density through the EIFRs. Bio-cluster developments are impossible to predict, yet clustering can be used as a long-term target on which sectoral development initiatives can be orientated.

The study also demonstrates that development initiatives should ultimately seek to focus on developing place specific forms of competitive advantage in niche areas through exploiting the opportunities that Post-Fordism and biotechnology present. By tailoring their policy initiatives towards their local strengths to develop 'niche' areas in which they possess/can develop competitive advantage(s), non-hub sectors can address the formation of a global mass of diagnostic and platform technology firm developments, which has emerged due to the main focus of the international bio-sector being on pharma-biotechnology related developments.

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APPENDIX A:
QUESTIONNAIRE AND EXPLAINATION

A.1 QUESTIONNAIRE

Networks in the Irish Biotechnology Industry

Questionnaire Survey

NUI MAYNOOTH

Ollscoil na hÉireann Má Nuad

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta

Irish Research Council for the Humanities and Social Sciences

IRCHSS

NIRSA

NATIONAL INSTITUTE FOR REGIONAL AND SPATIAL ANALYSIS

START HERE

Q.1 What is the name of your firm/plant?

Q.2 What is the nationality of this firm/plant?

Q.3 How many people does this firm/plant employ?

Q.4 Of this number, what proportion are scientists/technologists?

Q.5 In the following table, please list your firm's/plant's main products in the first column, and for each, indicate (approximately) the proportion of that product's output which goes to each of the indicated market categories.

Products	Market category	% of output
Product 1:	Consumer market	
	Corporate market	
	Further processing	
	Other (Specify)	
Product 2:	Consumer market	
	Corporate market	
	Further processing	
	Other (Specify)	
Product 3:	Consumer market	
	Corporate market	
	Further processing	
	Other (Specify)	

Q.6 Where products are sold to other firms for further processing, are these:
(a) standard commercial contracts?
Yes ☐ No ☐
(b) OR do any involve some form of special collaborative arrangement?
Yes ☐ No ☐

If you answer No for either part, please give details.

Q.7 In the following table, please indicate if any of your main products are produced with outside collaboration.

Form of collaboration	Details
Other biotechnology firm*	
International corporation*	
University	
Research Institute	
Other (please specify)	

* **"biotechnology firm" refers to a specialised biotechnology firm.**
* **"international corporation" refers to a large corporation, typically with a pharmaceutical or biopharmaceutical division, which operates on an international scale.**

Q.8 In the following table, list your firm's main inputs (in value terms) and where they are sourced (as indicated). Inputs include both materials and services.

Input	Type of input	Mainly sourced in Ireland?				If not Ireland, where is input sourced?
1		Yes		No		
2		Yes		No		
3		Yes		No		
4		Yes		No		
5		Yes		No		

Q.9 Are any of your inputs supplied through collaborative arrangements with other firms or institutions (please give details, including locations/nationalities of other firms/institutions)?

Q.10 Is your firm engaged in any other collaborative arrangements apart from those covered by earlier questions?

To assist in answering this question, four separate tables follow referring, respectively, to Other Biotechnology Firms, International Corporations, Universities and Research Institutes.

Please complete each table as appropriate:

(A) COLLABORATIONS WITH OTHER BIOTECHNOLOGY FIRMS		
Names/locations of firms	**Firm's name**	**Location (country)**
	1	
	2	
	3	
How long has your firm been collaborating with each of these firms?	**1**	
	2	
	3	
What is the nature of your firm's relationship with these firms?	**1**	
	2	
	3	
If the nature of your firm's relationships with any of these firms has changed over time, please indicate the nature of these changes?	**1**	
	2	
	3	

(B) COLLABORATIONS WITH INTERNATIONAL CORPORATIONS		
Names/locations of Corporations	**Firm's name**	**Location (country)**
	1	
	2	
	3	
How long has your firm been collaborating with each of these Corporations?	**1**	
	2	
	3	
What is the nature of your firm's relationship with these Corporations?	**1**	
	2	
	3	
If the nature of your firm's relationships with these Corporations has changed over time, please indicate the nature of these changes?	**1**	
	2	
	3	

(C) COLLABORATIONS WITH OTHER UNIVERSITIES		
Names/locations of Universities	**Firm's name**	**Location (country)**
	1	
	2	
	3	
How long has your firm been collaborating with each of these Universities?	**1**	
	2	
	3	
What is the nature of your firm's relationship with these Universities?	**1**	
	2	
	3	

Continued on the following page

If the nature of your firm's relationships with these Universities has changed over time, please indicate the nature of these changes?	**1**	
	2	
	3	

(D) COLLABORATIONS WITH OTHER RESEARCH INSTITUTES		
Names/locations of Institutes	**Firm's name**	**Location (country)**
	1	
	2	
	3	
How long has your firm been collaborating with each of these Institutes?	**1**	
	2	
	3	
What is the nature of your firm's relationship with these Institutes?	**1**	
	2	
	3	
If the nature of your firm's relationships with these Institutes has changed over time, please indicate the nature of these changes?	**1**	
	2	
	3	

Q.11 Has your firm experienced any difficulties in forming alliances/collaborations with other firms/institutions?

Yes ☐ **No** ☐

If Yes, please elaborate.

Q.11b What do you think needs to be done to get over such difficulties?

Q.12 Has your firm's ownership structure changed since its foundation?
Yes ☐ **No** ☐

If yes, please indicate the nature of the change from the following table:

	Details
Internal change of ownership	
Partial takeover by international corporation	
Complete takeover by international corporation	
Partial takeover by other biotech firm	
Complete takeover by other biotech firm	
Merger with other firm	
Joint venture with other firm	
Other	

Q.13 Have Venture Capital funds played a role in the formation/development of your firm?

Yes ☐ **No** ☐

If Yes, please elaborate on their role.

Q.14 Does being located in Ireland create any operational problems for your firm?

Yes ☐ **No** ☐

If Yes, please elaborate.

Q.15 In your opinion, what are the issues that need to be addressed in order for the Irish biotechnology sector to optimise its potential?

Thank you for your co-operation and for taking the time to fill out this survey.
Please return the survey in the enclosed S.A.E. or send it to:

John O'Byrne,
Dept. of Geography,
N.U.I. Maynooth,
Maynooth,
Co. Kildare

Please be assured that the contents of this survey will be treated in strict confidence. If you have any queries, please do not hesitate to contact me at
john.p.obyrne@nuim.ie **or at 01 7086208**

A.2 QUESTIONNAIRE STRUCTURE AND CONTENT

The following section presents the sequence of questions used in the questionnaire, and the rationale underlying these questions.

Q. 1 What is the name of your firm/plant?

While the identity of the biotechnology firm (bio-firm) in question would have been determined before the survey was issued, the rationale behind this question was to gently lead the respondent into the questionnaire. It was also included to establish if any changes of name had occurred, which might indicate a change of ownership, and allowed for an up-to-date list of the bio-firms comprising the indigenous biotechnology sector (bio-sector) to be completed.

Q. 2 What is the nationality of this firm/plant?

Prior to the issuing of the survey, it was assumed that the vast majority of the bio-firms surveyed would be Irish-owned. However, limited information existed to support this assumption. This question sought to establish just how many of the bio-sector's bio-firms were indeed Irish-owned.

Q. 3 How many people does this firm/plant employ?

Literature on the indigenous biotechnology sector's bio-firms, in particular the InterTradeIreland report, portrayed them as being small in size with an average of 20 employees per firm. No detailed figures beyond sectoral averages, or breakdowns in activity-based employment trends were presented in the available literature. This question sought to establish more detailed information on firm employment numbers, to identify possible employment patterns, and to establish whether any significant sectoral employment developments had occurred.

Q. 4 Of this number, what proportion are scientists/technologists?

A bio-firm with a high proportion of scientists/technologists would reflect a high level of research being conducted by that firm. This question sought to establish more detailed information on firm employment numbers, yet in particular sought to identify whether the indigenous bio-firms were still heavily engaged in research, as had been indicated in the literature pertaining to the sector, or whether any significant changes had occurred in this respect.

Q. 5 In the following table, please list your firm's/plant's main products, and for each, indicate (approximately) the proportion of that product's output which goes to each of the indicated market categories.

Details on three products were asked for, and the four market categories used were: Consumer market; Corporate market; Further processing; and Other (Specify). The amount asked was in "% of output".

This question sought to establish the stage in the production process (as detailed in chapter 3) occupied by the respondent bio-firms. The literature on the indigenous sector indicated that a very limited number of products were being produced in the indigenous sector, and that these were mainly to be found among the diagnostic bio-firms. Where products were being produced, this question also sought to determine the target markets for these products. From the four categories it would be possible to identify formal downstream linkages firms had established in the bio-sector, a task that would have been

impossible relying on existing literature. This information would then be used in the interview stage of the project.

Q. 6 Where products are sold to other firms for further processing, are these: (a) standard commercial contracts, or (b) do any involve some form of special collaborative agreement?
Yes/No options were provided for both parts. If the respondent answered "No" to either part, space was provided for the respondent to elaborate.

As information on specific collaborative arrangements was difficult to find in the literature on the sector, this question sought to establish the forms/types of formal arrangements/collaborations which bio-firms had formed where products were being produced. Space was provided for the respondent to detail any other arrangements that may have been set up between the respondent bio-firm and its collaborators. This question, once again, would allow for a more informed interview stage/process.

Q. 7 In the following table, please indicate if any of your main products are produced with outside collaboration?
Five outside collaborator types were listed as options: Other Biotechnology Firms; International Corporation; University; Research Institute; and Other (please specify).
Definitions of what was meant by "Biotechnology Firm" and "International Corporation" were provided to remove/reduce possible ambiguity in interpretation.

The five choices presented to the respondent were perceived as being the more likely formal collaborators available to the indigenous bio-firms, based on the completed sectoral profile and the actor typologies developed by Barley et al. (1992). Space was provided to allow the respondent to detail the form(s) of the collaboration(s).

Q. 8 In the following table, list your firm's main inputs (in value terms) and where they are sourced (as indicated). Inputs include both materials and services.
Five input categories were provided for ("Type of input"). These five inputs (details to be identified by the respondent) were individually queried: "Mainly sourced in Ireland, Yes/No; If not in Ireland, where is input sourced?"

As little information existed on how dependent Irish bio-firms were/are on indigenous inputs, this question sought to establish how interlinked the surveyed bio-firms were with other indigenous sectors. Identifying the main inputs of the bio-firms and where these were sourced would identify areas of strength or weakness in the indigenous sector, e.g. whether specific inputs were consistently being sourced indigenously, or outside of Ireland. The value of the inputs was sought in order to identify any major trends regarding the inputs sourced abroad or in Ireland. In asking where non-Irish inputs were sourced, follow-up questions in the interview process were to be conducted to establish the rationale behind the input sourced used.

Q. 9 Are any of your inputs supplied through collaborative arrangements with other firms or institutions (please give details, including locations/nationalities of other firms/institutions)?

Collaborative inputs would indicate that the respondent firms required specialist inputs, and would also allow the identification of vital formal collaborations/alliances that the bio-firms had established. This question provided space for the respondent to elaborate. In the cases where a basic answer was provided, a follow-up question was to be included in the interview process.

Q. 10 Is your firm engaged in any other collaborative arrangements apart from those covered by earlier questions?
To assist in answering this question, four separate tables followed referring, respectively, to Other Biotechnology Firms, International Corporations, Universities and Research Institutes.

Existing information on collaborative arrangements in the sector is minimal. Answers to this question were categorised according to the four main actor types in the sector's innovation process, as identified by Barley et al. (1992). The decision to limit the actor options was based on discussions with individuals with extensive sector knowledge. For each category, information was sought on collaborators, their country of origin (to measure Ireland's interconnectedness with the global sector), the nature of the collaboration, and whether the form of collaboration had changed over time to see if trends, such as increased interdependence, were apparent in the bio-sector.

Q. 11 Has your firm experienced any difficulties in forming alliances/collaborations with other firms/institutions?
Yes/No options were provided. If the respondent answered "Yes", they were asked to elaborate.

This question sought to detail issues which the respondent bio-firms faced in forming alliances/collaborations. This information would be vital in gaining a full understanding of the workings of the bio-sector and would identify issues requiring further investigation. Allowing the respondent to elaborate would facilitate the specific detailing of issues that affected the bio-firm, and would potentially identify general sectoral issues.

Q. 11b What do you think needs to be done to get over such difficulties?
Space was supplied to allow the respondent elaborate.

The second part of this question sought to identify possible solutions the respondents might have for addressing the issues raised by the first part of the question. This part of the question would then provide possible avenues of investigation in the interview stage of the project.

Q. 12 Has your firm's ownership structure changed since its foundation?
Yes/No options were provided. If the respondent answered "Yes", they were asked to indicate the nature of change from a table that contained eight options:

- Internal change of ownership,
- Partial takeover by international corporation,
- Complete takeover by international corporation,
- Partial takeover by other biotechnology firms,
- Merger with another firm,

- Joint venture with another firm, and
- Other.

Space was provided for the respondent to elaborate.

It was important to establish the details regarding changes to a bio-firms' ownership structure. This information would highlight if a bio-firm was autonomous or if its activities were decided by another actor. In the cases where a respondent bio-firm indicated a change in ownership, a follow-up question was included in the interview stage of the research.

Q. 13 Have Venture Capital funds played a role in the formation/development of your firm?
Yes/No options were provided. If the respondent answered "Yes", space was provided to allow the respondent to elaborate.

VC involvement in the indigenous bio-sector, according to the literature reviewed, is limited. The question sought to establish the overall level of VC involvement in the indigenous sector, and, where possible, identify if involvement came from foreign VC sources.

Q. 14 Does being located in Ireland create any operational problems for your firm?
Yes/No options were provided. If the respondent answered "Yes", space was provided to allow the respondent to elaborate.

Q. 15 In your opinion, what are the issues that need to be addressed in order for the Irish biotechnology sector to optimise its potential?
Space was provided to allow the respondent elaborate.

Once again, as literature on sectoral weaknesses is limited, this question sought to identify pressing or general sectoral issues with which the survey bio-firms were confronted.

APPENDIX B:
LETTERS AND OTHER CONTACTS WITH TARGET BIOTECHNOLOGY FIRMS

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

Dear Mr. Doe

I am currently conducting a study of networks and interlinkages between firms in the Irish biotechnology industry. International studies have highlighted the importance of such networks and linkages in the development of the industry. This study, which is sponsored by the National Institute for Regional and Spatial Analysis (NIRSA), seeks to optimize the development of the biotechnology industry in Ireland through enhancing the formation and functioning of networks among the sector's actors.

As part of this study, I will be sending you, in the next few days, a questionnaire survey form relating to your own firm's networking arrangements. I would be very grateful if you would take the time to complete this survey which will assist in the formulation of effective policies for the development of the Irish biotechnology industry.

Thank you for your time and consideration. I look forward to receiving your assistance in the completion of this study.

Yours sincerely,

_____

John O'Byrne
Doctoral Research Fellow, NIRSA

NUI MAYNOOTH
Ollscoil na hÉireann Má Nuad

Tel: +353 (0)1 **7086208**
E Mail: john.p.obyrne@nuim.ie

National University of Maynooth
Co. Kildare, Ireland

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

Biotechnology Company
Ireland

Dear Mr. Doe

In the last few days you should have received a letter from me requesting your assistance in completing a questionnaire survey relating to networks in the Irish biotechnology industry. This study is sponsored by the National Institute for Regional and Spatial Analysis (NIRSA), and is primarily aimed at optimizing the development of the biotechnology industry through enhancing the formation and functioning of networks among the sector's actors. As you will know, biotechnology has been identified by the Irish government as playing a key role in the future development of the Irish economy.

The survey is concerned with collaborative or networking arrangements that may exist between your firm and other actors in the biotech industry. Such arrangements are formed in order to achieve shared objectives or benefits and include (for example) joint marketing or the exchange of skills, equipment, and information. The survey mainly consists of a series of open-ended questions that allow you to elaborate on your firm's specific experiences in forming networks with sector actors in the Irish biotechnology industry.

I would be very grateful if you could take the time to complete the enclosed survey form. The successful completion of this study is dependent on you completing this survey and sharing your experiences of working within the Irish biotechnology sector. Completion of the survey should take no more than 10 minutes. Your answers will be kept **completely confidential** and the survey results will be released only in summary form so no individual's answers can be identified.

If you have any questions or comments about this study, I would be happy to talk with you. You can contact me at the addresses or number on the letterhead. A summary of the survey findings will be sent to all participating firms.

Thank you very much for helping us with this important study.

Yours sincerely,

_____

John O'Byrne
Research Fellow, NIRSA

NUI MAYNOOTH
Ollscoil na hÉireann Má Nuad

Tel: +353 (0)1 **7086208**
E Mail: john.p.obyrne@nuim.ie

National University of Maynooth
Co. Kildare, Ireland

3rd August, 2004

NUI MAYNOOTH

Last month a survey form on networks in the Irish biotechnology sector was posted to you.

If you have already completed and returned the survey to me, please accept my sincere thanks. If not, could you please do so today. I am especially grateful for your help because it is only through you, sharing your experiences of networks among Irish biotechnology firms that this study can be successfully completed.

If you did not receive a survey form, or it was misplaced, please call me at 01-7086208 or e-mail me at john.p.obyrne@may.ie and I will get another one in the post to you today.

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

John O'Byrne
Research Fellow
NIRSA
NUI Maynooth
Co. Kildare

National University of Maynooth
Co. Kildare, Ireland

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

Dear Mr. Doe

I am writing to you to thank you for completing my questionnaire survey form (relating to your own firm's networking arrangements) which I sent out to you over a month ago. I gratefully appreciate your response.

Please note that your answers will be kept **completely confidential** and the survey results will be released only in summary form so no individual's answers can be identified.

If you have any questions or comments about this study, I would be happy to talk with you. A summary of the survey findings will be sent to all participating firms.

Thank you very much for helping with this important study.

Yours sincerely,

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John O'Byrne
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I would be very grateful if you could take the time to complete the enclosed survey form. The successful completion of this study is dependent on you completing this survey and sharing your experiences of working within the Irish biotechnology sector. Completion of the survey should take no more than 10 minutes. Your answers will be kept completely confidential and the survey results will be released only in summary form so no individual's answers can be identified.

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Thank you very much for helping us with this important study.

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John O'Byrne
Research Fellow, NIRSA

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An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

Dear Mr. Doe,

My name is John O'Byrne, I am currently engaged in research for my PhD thesis entitled "Networks and the development of the Irish biotechnology sector" at the NUI, Maynooth.
My study, which is sponsored by the Irish Research Council for the Humanities and the Social Sciences (IRCHSS) and the National Institute for Regional and Spatial Analysis (NIRSA), seeks to optimise the development of the biotechnology industry in Ireland through enhancing the formation and functioning of networks among the sector's actors.
I am presently conducting a study of networks and interlinkages between universities and the Irish biotechnology industry, and as such, I would like to interview key university staff members who are involved in collaborations/alliances (research based, or otherwise) with biotechnology firms, corporations (e.g. pharmaceutical companies) and other universities.
I am curious if it would be possible for me to set up an interview with you to explore your experiences in facilitating University/biotechnology firm alliances/collaborations?
Please note that any information received during any correspondence will be treated with the utmost confidentiality.

Yours sincerely,
John O'Byrne

Doctoral Research Fellow

Irish Research Council for the Humanities and the Social Sciences
http://www.irchss.ie/

National Institute for Regional and Spatial Analysis
http://www.nuim.ie/nirsa/

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Tel: +353 (0)1 **7086208**
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Co. Kildare, Ireland

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My study, which is sponsored by the Irish Research Council for the Humanities and the Social Sciences (IRCHSS) and the National Institute for Regional and Spatial Analysis (NIRSA), seeks to optimise the development of the biotechnology industry in Ireland through enhancing the formation and functioning of networks among the sector's actors.
I am presently conducting a study of networks and interlinkages that exist between indigenous biotechnology companies and the Irish biotechnology industry.
As such, I would like to interview key firm members who are involved in collaborations/alliances (research based, or otherwise) with university based researchers, corporations (e.g. pharmaceutical companies) and other indigenous biotechnology firms.
I am curious if it would be possible for me to set up an interview with you to explore your experiences in relation to your firms networking activities?
Please note that any information received during any correspondence will be treated with the utmost confidentiality.

Yours sincerely,
John O'Byrne

Doctoral Research Fellow

Irish Research Council for the Humanities and the Social Sciences
http://www.irchss.ie/

National Institute for Regional and Spatial Analysis
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Dear Mr. Doe,

My name is John O'Byrne, I am currently engaged in research for my PhD thesis entitled "Networks and the development of the Irish biotechnology sector". My study, which is sponsored by the Irish Research Council for the Humanities and the Social Sciences (IRCHSS) and the National Institute for Regional and Spatial Analysis (NIRSA), seeks to optimise the development of the biotechnology industry in Ireland through enhancing the formation and functioning of networks among the sector's actors.
I am presently conducting a detailed study of existing networks and interlinkages between all sectoral actors in the domestic biotechnology sector, and as such, I would like to interview key staff members of agencies that are involved in the sector.
I am curious if it would be possible for me to set up an interview in order to explore your experiences/views/opinions in relation to the domestic biotechnology sector?
Please note that any information received during any correspondence will be treated with the utmost confidentiality.

Yours sincerely,
John O'Byrne

Doctoral Research Fellow

Irish Research Council for the Humanities and the Social Sciences
http://www.irchss.ie/

National Institute for Regional and Spatial Analysis
http://www.nuim.ie/nirsa/

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APPENDIX C:
BIOTECHNOLOGY/BIOTECHNOLOGY-RELATED DEPARTMENTS IN IRISH UNIVERSITIES

This appendix details and discusses the various biotechnology/biotechnology-related departmental and educational activities conducted by Irish university biotechnology/biotechnology-related departments and faculties.

There are eight Universities in Ireland:

- Dublin City University (DCU)
- University College Cork (UCC)
- University College Dublin (UCD)
- National University of Ireland Galway (NUIG)
- National University of Ireland Maynooth (NUI, Maynooth)
- Trinity College Dublin (TCD)
- the University of Limerick (UL), and
- the Royal College of Surgeons, Ireland

C.1 DUBLIN CITY UNIVERSITY

Founded in 1980 as a technical college, Dublin City University (DCU) was awarded university status in 1989. DCU was the first Irish University to establish an undergraduate degree in Biotechnology in the mid 1980s (Dublin City University, 2005).

C.1.1 DCU Faculties

C.1.1.1 Faculty of Science and Health

The six schools of DCU's Faculty of Science and Health's teaching and research activities are inter-disciplinary focused. Among the teaching aspect of the various faculty school programmes are physical and biological sciences (Dublin City University, 2007a).

C.1.1.1.1 School of Biotechnology

DCU's School of Biotechnology incorporates teaching and research facilities in a single departmental unit for Process Engineers, Biochemists, Microbiologists, Geneticists and Pharmacologists. The school has established basic and applied research collaborative links with national and international research laboratories and has developed close alliances with DCU based research centres (discussed in further detail in Appendix D) such as the National Institute for Cellular Biotechnology (NICB) and the National Centre for Sensor Research (NCSR) (Dublin City University, 2005).

The School's undergraduate programme includes four year B.Sc. degrees in Biotechnology, Environmental Science & Health, and Genetics and Cell Biology. The School's postgraduate degree programmes include a M.Sc. in Bioinformatics, and a GDip/MSc in Biomedical Diagnostics (Dublin City University, 2007b, 2007c, 2007d, 2007e, 2007f).

C.1.1.1.2 School of Chemical Sciences

The School of Chemical Sciences research activities include environmental and analytical chemistry, combinatorial synthesis, nanotechnology, photochemistry and spectroscopy research programmes. Close research collaborations have developed between the school and the NICB and the NCSR. The School's teaching programmes

include B.Sc. degrees in Analytical Science, Chemical and Pharmaceutical Sciences (Dublin City University, 2007g, 2007h, 2007i).

C.2 UNIVERSITY COLLEGE CORK

University College Cork (UCC) was founded in 1845 and is the second largest university in Ireland (University College Cork, 2007).

C.2.1 UCC Faculties

UCC's College of Science, Engineering and Food Science comprises of the Faculties of Science, Engineering, and Food Science and Technology (University College Cork, 2006a).

C.2.1.1 The Faculty of Science

UCC's Faculty of Science includes the Departments of Biochemistry, Chemistry, Microbiology, Zoology, Ecology, and Plant Science (University College Cork, 2007).

C.2.1.1.1 The Department of Biochemistry

Established in 1945, the Department of Biochemistry is engaged in molecular and cellular education, training and research. The Department of Biochemistry's undergraduate programmes include a four year B.Sc. in Biochemistry, this degree focuses on the biological and chemical sciences. The degree involves courses on Structural Biochemistry, Membrane Biochemistry, Cell Signalling, Biochemical Immunology, Principles of Medical Genetics, and Bioinformatics. The Department it is also involved in the Biomedical Sciences degree, the BSc in Genetics, the preclinical years of the medical degree (MB, BCh, BAO), dental degree (BDS) courses in the medical foundation year, and the BSc in chemistry of pharmaceutical compounds. The Department's postgraduate degree programmes include Higher Diploma in Applied Science (Biotechnology), and a M.Sc. degree in Applied Science (Biotechnology) (University College Cork, 2003a, 2006b)

C.2.1.1.2 The Department of Microbiology

The Department of Microbiology is a member of two UCC Faculties, the faculty of Science and Food Science and Technology and the Faculty of Medicine. The Department has established close research and teaching ties with UCC departments, including the Department of Food Science and Technology, the Department of Medicine. Extensive collaborations have developed with Teagasc's Dairy Products Centre in Moorepark, Fermoy. The department's research programmes include topics in Genomics and Molecular Biology (University College Cork, 2005).

The Department's undergraduate programme includes a B.Sc. in Biology that has six possible specialisations: Microbiology, Plant and Microbial Biotechnology, Biomedical Sciences, Food Sciences, Food Technology, and Genetics. The Department's postgraduate degree programmes include a research based M.Sc. degree. This is based upon a research project completed under the supervision of a faculty member (University College Cork, 2005).

C.2.1.1.3 The Department of Zoology, Ecology, and Plant Science

The Department of Zoology, Ecology, and Plant Science (ZEPS) was formed in 2002 with the amalgamation of UCC's Departments of Zoology and Animal Ecology, and Plant Science. The Department's research activities are in the areas of marine, terrestrial and freshwater animal/plant ecology, environmental plant biotechnology, and population

genetics (University College Cork, 2003b).

The Department's undergraduate degree programmes include B.Sc. degrees in Zoology, Applied Ecology, and Environmental Plant Biotechnology. The Department's postgraduate degree programmes include s a two year M.Sc. in Ecosystem Conservation and Landscape Management (University College Cork, 2007, 2006c).

C.2.1.2 The Faculty of Food Science and Technology

The Faculty of Food Science and Technology's activities are focuses on the areas of Dairy and Food Science education and research, including Food Biotechnology. There are 5 Departments in the Faculty including the Departments of Food, Business and Development, Microbiology (discussed above), Food and Nutritional Science, and Process and Chemical Engineering. The Faculty has developed close connections with the National Food Biotechnology Centre (NFBC) (University College Cork, 2006a).

C.2.1.2.1 The Department of Food, Business and Development

The Department is focused on research relating to the agri-food industry, including developing current agricultural practices, to food processing. The research activities of the Department are focused on three general topics, Food Business, co-operative Business, and Rural Development.

The Department's undergraduate programmes include a 2 year B.Sc. in Food Business. This degree combines Food Business and Food Science and Technology courses. Business and marketing skills are combined with knowledge of food products and processes. The Department's postgraduate degree programmes include a range of postgraduate courses and research programmes are offered by the department. Ph.D. and MSc research programmes in Food Chemistry, Food Economics, Food Engineering, Food Technology, Microbiology and Nutrition are available (University College Cork, 2007d, 2007e).

C.2.1.2.2 The Department of Physiology

The Department of Physiology brings together academics from the fields of physiology, pharmacology, biochemistry, molecular biology and clinical research. The Department's research involves programmes in the fields of Cell, Molecular and Integrative Physiology. Collaborative research projects are conducted with researchers from the Departments of Microbiology and Anatomy, and the Biosciences Research Institute (University College Cork, 2007f, 2007g).

C.3 UNIVERSITY COLLEGE DUBLIN

University College Dublin (UCD) was originally established in 1854. UCD is Ireland's largest university with 5 Colleges and 35 Schools. The University's biotechnology and biotechnology-related research is conducted in the Departments of Medicine, Veterinary Medicine and Agriculture as well the Department of Biochemistry, Industrial Microbiology, Botany, Zoology, Microbiology and Pharmacology, yet the main activity is carried out in the faculty of Science where research efforts focus on microbiology, molecular genetics, toxicology, immunology, drug design, biodiversity, industrial microbiology, pharmacology and zoology (Burke at al., 2003).

C.3.1 College of Engineering, Mathematical and Physical Sciences

There are 7 schools in the College of Engineering, Mathematical and Physical Sciences, including the School of Chemical and Bioprocess Engineering (University College

Dublin, 2007a).

C.3.1.1 The UCD School of Chemical and Bioprocess Engineering
The School of Chemical and Bioprocess Engineering is engaged in research in the areas of Bioprocess engineering, Cell biology, Biofilm Engineering, and Animal Cell Culture Technology. The School's teaching programmes include a 4 year B.E. in Chemical Engineering or Bioprocess Engineering and taught and research MEngSc degrees (University College Dublin, 2006, 2007b, 2007c).

C.3.2 The College of Life Sciences
The College of Life Science comprises eight scientific schools, and the UCD Veterinary Hospital (University College Dublin, 2007d).

C.3.2.1 School of Agriculture, Food Science and Veterinary Medicine
The school engages in research and teaching programmes focused on animal health and welfare, human health, food systems and agriculture. The School's undergraduate degree programmes include B.Sc. degrees in Food Science, Food & Agri-Business Management, Agri-Environmental Sciences, Animal & Crop Production, Animal Science, and in Engineering Technology. The School's postgraduate degree include research M.Sc. degrees in Science, Science (Agriculture), Agricultural Science, Animal Science, Engineering Science, and in Veterinary Medicine. The School also offers taught M.Sc. degrees in Engineering Science: Food Engineering, and Engineering Technology (University College Dublin, 2007e, 2007f, 2007g, 2007h).

C.3.2.2 UCD School of Biology and Environmental Science
The school engages in teaching and research in the areas of modern biology and environmental science, these include programmes in botany, cell and molecular biology, environmental science, genetics, and zoology. The school's research programmes cover a wide range of areas: general zoology, animal behaviour, biodiversity, bioremediation, cell biology, developmental biology, genetics, and marine fisheries (University College Dublin, 2007i).

C.3.2.3 UCD School of Biomolecular and Biomedical Science
The School brings together academics different disciplines including Biochemistry, Microbiology, Pharmacology and Physiology. The school's research and teaching programmes are focused biological systems at molecular, cellular and whole organism levels. The school is part of the Conway Institute of Biomolecular and Biomedical Research (University College Dublin, 2007j).

The School's undergraduate programmes include B.Sc. (Honours) and B.Sc. (General) degrees in Biochemistry, Microbiology, Pharmacology and Physiology. B.Sc. (Joint Honours) programmes are also available to prospective students, which can be combined with degrees in other disciplines including Chemistry and Molecular Genetics (University College Dublin, 2007k).

C.3.2.4 UCD School of Chemistry and Chemical Biology
The School is home to 24 research groups with interests spanning a wide range of chemical sciences. The School opened the Centre for Synthesis and Chemical Biology (CSCB) in 2005. The School of Chemistry and Chemical Biology's teaching programmes include a 4 year B.Sc. in Medicinal Chemistry & Chemical Biology that was introduced in 2007 (University College Dublin, 2007l, 2007m).

C.3.2.5 UCD School of Medicine and Medical Science

The School has developed clinical research programs in six Dublin partner hospitals:

- the Mater Misericordiae University Hospital;
- St. Vincent's University Hospital;
- the National Maternity Hospital;
- the Coombe Women's Hospital;
- Our Lady's Hospital for Sick Children; and
- the Children's University Hospital at Temple Street.

The school's research programmes range from fundamental biology through translational research to population and clinical research. The school has extensive collaborations with the Conway Institute of Biomolecular and Biomedical Sciences and the Dublin Molecular Medicine Centre. The School's teaching programmes include a B.Sc. in Biomedical Health and Life Sciences as well as taught and research postgraduate level M.Sc. degrees (University College Dublin, 2007n, 2007o).

C.4 NATIONAL UNIVERSITY OF IRELAND, GALWAY

The National University of Ireland at Galway (NUIG) was originally founded in 1845, and became one of the National Universities of Ireland in 1997 (National University of Ireland, Galway, 2007a).

C.4.1 The Faculty of Medicine, Nursing, and Health Sciences

C.4.1.1 The Department of Bacteriology

The Department hosts the National Salmonella Reference Laboratory for Ireland, while its research activities include Antimicrobial Resistance in Human and Animal Pathogens. The department is closely associated with the Department of Medical Microbiology at NUIG's University College Hospital. The Department of Bacteriology's Bacteriology course begins in the final term of the Third Medical year. The Department also runs a Mechanisms of Disease course jointly with the Department of Pathology (National University of Ireland, Galway, 2007b, 2007c).

C.4.2 The Faculty of Science

The Faculty of Science's department include the Department of Biochemistry, Chemistry, Microbiology, and Pharmaceutical and Therapeutics. The faculty of science offers two types of B.Sc. degrees, the undenominated programme (a three year degree that has a general focus to allow students to identify the area they are most interested in) and the denominated programme (this has a specific focus and is four years long) (National University of Ireland, Galway, 2003, 2007d).

C.4.2.1 The Department of Biochemistry

The Department of Biochemistry was established in 1963. The department's activities involve activities in the areas of genetics, immunology, cell biology and structural biology. The Department's undergraduate programmes include a B.Sc. in Biochemistry. The Department of Biochemistry, in collaboration with the Departments of Microbiology and Medicine, offers a B.Sc. in Biotechnology. The B.Sc. in Biotechnology is a four year degree in which students specialise in one of the following subject areas: Anatomy, Physiology or Biochemistry. The degree also includes an annual ICT module, the aim being to produce graduates with the necessary skills needed in industry (National University of Ireland, Galway, 2007e, 2007f).

C.4.2.2 The Department of Chemistry
The Department of Chemistry was founded in 1849, its research activities include Environmental Chemistry, Chemical Synthesis, and Bioanalytical Chemistry. The Department offers a four year B.Sc. Programme, and a H.Dip. in Analytical Chemistry and Biochemistry (National University of Ireland, Galway, 2007g, 2007h).

C.4.2.3 The Department of Botany
The Department of Botany offers Botany B.Sc. degrees at general and honours level. The first year of the degree entails an extensive course in basic Biology (no prior knowledge of biology is necessary for students). The second and third years of the degree become more specialized in their focus. Only in the fourth year (when a student has qualified to complete an honours degree) is Botany studied exclusively. The Botany Department also contributes extensively to the Denominated B.Sc. Degrees in Marine and Environmental Science (National University of Ireland, Galway, 2007i).

C.4.2.4 The Department of Microbiology
The Department of Microbiology was established in 1965. The department's research focuses are in the areas of biotechnology, environmental microbiology, aquaculture, marine sciences, genetics and bacterial pathogenesis (National University of Ireland, Galway, 2007j).

C.4.2.5 The Department of Pharmacology
The Department was formed in 1974, its research activities focus on the central nervous system, in particular the mechanism of action of antidepressants and drugs of abuse. The Department's undergraduate programmes include courses on Medicine, and B.Sc. degrees in Biotechnology, Biomedical Science and Nursing (National University of Ireland, Galway, 2007k).

C.5 NATIONAL UNIVERSITY OF IRELAND, MAYNOOTH
The National University of Ireland at Maynooth (NUIM) was established as a university in 1997 (National University of Maynooth, 2007a).

C.5.1 The Faculty of Science & Engineering
C.5.1.1 The Department of Biology
Established in 1970, the Department of Biology has grown into one of the largest departments in the university. The Department of Biology's research focus is in the areas of Biological Control, Immunology, Medical Mycology, Molecular Genetics and Plant Biotechnology (National University of Maynooth, 2007b).

The Department of Biology offers prospective students several four year B.Sc. degree courses; a BSc (Single Honours)/ BSc (Double Honours) (in which students are educated in a wide educational range in modern biological activities, including Evolutionary Biology, Microbiology, Plant Biology, Bioethics and Biotechnology), a Denominated Honours Degree in Biotechnology, and Denominated Honours Degree in Genetics & Bioinformatics. The postgraduate degree options available through the department include a taught MSc in Immunology & Global Health, and research MSc and PhD degrees (National University of Maynooth, 2007c).

C.6 TRINITY COLLEGE DUBLIN
Trinity College Dublin (TCD) is Ireland's oldest university, being established in 1592. There are five academic faculties in TCD, two of which are related to biotechnology (Trinity College Dublin, 2007a).

C.6.1 The Faculty of Health Science

The Faculty of Health Sciences brings together four schools, the schools of Medicine, Dental Science, Pharmacy and Pharmaceutical Sciences, and Nursing and Midwifery. The faculty has close alliances with two Dublin teaching hospitals; St James's Hospital and the Adelaide and Meath Hospital, Dublin incorporating the National Children's Hospital (AMNCH) at Tallaght (Trinity College Dublin, 2007b).

C.6.1.1 The School of Pharmacy and Pharmaceutical Sciences

Established in 1977, the School of Pharmacy and Pharmaceutical Sciences offers prospective students a B.Sc. in Pharmacy, and several postgraduate degree types: M.Sc. and Diplomas in Pharmaceutical Manufacturing Technology and Pharmaceutical Analysis, and a M.Sc. in Pharmaceutical Technology (Trinity College Dublin, 2007c, 2007d).

C.6.2 The Faculty of Science

The Faculty of Science facilities include the East End Building, located on the main TCD campus. This building houses the School of Pharmacy, the Smurfit Institute of Genetics, and the Biology Teaching centre (Trinity College Dublin, 2007e).

C.6.2.1 The School of Biochemistry and Immunology

The School of Biochemistry and Immunology was established in 2005 through the joining of the existing disciplines of Biochemistry and Immunology. The school's research programmes include Folic Acid Biochemistry, Structural Biology, Neurochemistry, Biotechnology and Vaccines. The school offer three undergraduate degree programmes to prospective students in Biochemistry with Structural Biology, Biochemistry with Cell Biology and Biochemistry with Immunology. The School also offers a research M.Sc. (Trinity College Dublin, 2007f, 2007g, 2007h, 2007i).

C.6.3 The Vice-Deanery of Genetics & Microbiology

This Vice-Deanery of Genetics & Microbiology comprises the Smurfit Institute of Genetics, and the Department of Microbiology (Trinity College Dublin, 2007j).

C.6.3.1 The Smurfit Institute of Genetics

Established in 1998, the research and teaching programmes of the Institute of Genetics encompasses molecular, cellular, developmental, behavioural, medical, psychiatric, population and quantitative genetics. The institute offers two B.A. undergraduate degree programmes in Genetics and Human Genetics (Trinity College Dublin, 2007k, 2007l).

C.6.3.2 The Department of Microbiology

The Department's research topics include molecular biology of pathogenic microbes, preventive medicine, and microbial systems biology. The Department has established extensive research alliances with the Unit of Clinical Microbiology at St. James's Hospital. The Department's undergraduate programme is a 4 year B.A. in Microbiology. The Department's postgraduate programmes include research M.Sc. and Ph.D. programmes (Trinity College Dublin, 2007m).

C.7 UNIVERSITY OF LIMERICK

The University of Limerick (UL) was established in 1972, it became a university in 1989 (University of Limerick, 2006).

C.7.1 The College of Science

The College of Science includes extensive teaching and research programmes in a wide range of scientific areas including Biochemistry, Environmental Sciences, Pharmaceutical and Industrial Chemistry, and Food Science & Health. The College's research focus includes the environment and biosciences (University of Limerick, 2007a).

C.7.1.1 The Department of Chemical & Environmental Sciences
The Department's research activities include electrochemistry, organic chemistry and industrial biochemistry. The Department offers undergraduate B.Sc. degree courses in Pharmaceutical and Industrial Chemistry, Industrial Biochemistry, and Environmental Science (University of Limerick, 2003: 2007b).

C.7.1.2 The Department of Life Sciences
The Department BSc degree courses in Food Technology, and Equine Science (University of Limerick, 2007c, 2007d).

C.8 THE ROYAL COLLEGE OF SURGEONS, IRELAND

The Royal College of Surgeons (RCSI) was established in 1784. Since 1977 it has recognised as one of the National University of Ireland colleges (Royal College of Surgeons, Ireland, 2007a, 2007b).

C.8.1 The School of Medicine and Health Sciences

C.8.1.1 The Department of Clinical Microbiology
The Department of Clinical Microbiology was established in 1965, it is located in the RCSI Education and Research Centre and the Smurfit Building on the Beaumont Hospital campus. The department's research programmes includes basic and clinical research, with particular focus on the genetics of bacterial virulence factors and the surveillance and treatment of antibiotic resistant pathogens. The department conducts undergraduate and postgraduate teaching of medical, pharmacy and nursing students (Royal College of Surgeons, Ireland, 2003).

C.8.1.2 The Department of Molecular and Cellular Therapeutics
The Department was established in 2006 through the amalgamation of the Departments of Biochemistry and Clinical Pharmacology. The Department is engaged in wide reaching teaching and research programmes that cover the preclinical and clinical domains of the college. The Department is located on the main RCSI campus and additional facilities at Beaumont Hospital. The Department's research activities include molecular and population genetic aspects of inherited disease, metabolic diseases, cardiovascular medicine and neuroscience (Royal College of Surgeons, 2007c).

C.8.2 The School of Pharmacy

The School is engaged in biopharmaceutical science research, and offers a four year B.Sc. in Pharmacy as well as a M.Sc. in Industrial Pharmaceutical Sciences (Royal College of Surgeons, 2007d).

APPENDIX D:
BIOTECHNOLOGY/BIOTECHNOLOGY-RELATED THIRD LEVEL RESEARCH INSTITUTES

This appendix details and discusses the various biotechnology/biotechnology-related research institutes (RIs) that are located in Ireland's Universities (Part A), and Institutes of Technology (Part B), and the main biotechnology-related research and teaching hospitals affiliated to Irish universities (Part C), as mentioned in Chapter 6.

D.1 UNIVERSITY RESEARCH INSTITUTES

D.1.1 Dublin City University

D.1.1.1 The National Cell and Tissue Culture Centre

The National Cell and Tissue Culture Centre (NCTCC) was established in 1987. It is one of the five Enterprise Ireland Biotechnology Directorate (EIBD) RIs. The centre's research focus is on animal cell biotechnology, its basic and applied research activities include Multi-drug resistance research, Cell Therapy & Tissue Engineering, Monoclonal and polyclonal antibody development, and In vitro screening of pharmacological agents. As with all of the EIBD RIs, one of the stated objectives of the centre is to commercialise its research through patenting commercial orientated research and through developing close interlinkages with indigenous and international firms. The NCTCC's research has led to the development of one indigenous biotechnology firm (bio-firm) spin-out, Archport (National Cell and Tissue Culture Centre, 2003a).

Several research groups have been established as off shoots from the NCTCC:

- The NCTCC Immunology Group: this group is engaged in research to develop and produce polyclonal and monoclonal antibodies,
- The NCTCC In Vitro Toxicology Group: this group specialises in cell culture and toxicology,
- The NCTCC Differentiation & Proteomics Group: this group is engaged in researching the process through which lung cells acquire their definitive form and function,
- The NCTCC Molecular Biology Group: this group is focused on the modelling and prediction of biological processes through the use of recent computer hard- and soft-ware developments.
- The NCTCC Diabetes Group: this group is engaged in research to find new treatments for type I diabetes through cell generation (National Cell and Tissue Culture Centre, 2003b, 2003c, 2003d).

D.1.1.2 The National Agriculture and Veterinary Biotechnology Centre

The National Agriculture and Veterinary Biotechnology Centre was established in 1987 as one of the five BioResearch Ireland RIs. Its research focus is on genomics, neurobiology, plant biotechnology, fungal biotechnology and vaccines (BioResearch Ireland, 2001j).

D.1.1.3 The National Institute for Cellular Biotechnology

The National Institute for Cellular Biotechnology (NICB) was established in 2002. Its partner institutes are the National University of Ireland, Maynooth (NUIM), and the IT Tallaght, and draws together researchers from the fields of Cellular Biotechnology, Molecular Cell Biology and Biological Chemistry, and Computer scientists. The NICB is engaged in cellular research at the molecular level, the institute's research

programmes aim to develop new therapeutic targets and diagnostic methods for specific diseases such as cancer, microbial diseases and diabetes (Dublin City University, 2004: Higher Education Authority, 2006).

D.1.1.4 The National Centre for Sensor Research

The National Centre for Sensor Research was established in 1999 through funding from the Programme for Research in Third Level Iinstitutes (PRTLI), the National Development Plan (NDP) and the European Union (EU). Its partner institute is the IT Tallaght. It is a multidisciplinary RI that brings together physicists, chemists, biotechnologists and mechanical engineers in eight research clusters (Dublin City University, 2004: Higher Education Authority, 2006).

D.1.1.5 The Materials Processing Research Centre

The Materials Processing Research Centre (MPRC) was founded 1990. The Centre is engaged in collaborative research with the University's School of Mechanical & Manufacturing Engineering. The centre is engaged in basic and applied material science and material processing technique research. Among its research programmes is the Polymers and Biomedical Devices programme (Materials Processing Research Centre, 2004a, 2004b).

D.1.1.6 The Vascular Health Research Centre

The Vascular Health Research Centre was established in 2005 through funding received from the Wellcome Trust, the US Department of Health and Human Services National Institutes of Health, the American Heart Association, and the (Irish) Health Research Board. The centre's research focus is in the areas of Vascular and developmental biology, Vascular disease and diabetes, and Vascular genomics and proteomics. The centre aims to develop new therapeutic treatments to address diseases using molecular and cellular biology techniques, in combination with functional genomics and proteomics strategies (Dublin City University, 2005).

D.1.1.7 The Centre for Bioanalytical Science

The Centre for Bioanalytical Science was established in 2007 as a joint-venture between Dublin City University (DCU), the National University of Ireland, Galway (NUIG) and Bristol-Myers Squibb. The centre was established to facilitate collaborations between research teams in the National Centre for Sensor Research, the National Institute for Cellular Biotechnology, and DCU's Schools of Biotechnology and Chemical Sciences. The Centre's research focus is in the area of bio-fermentation processes (Dublin City University, 2005).

D.1.1.8 The Biomedical Diagnostic Institute

The Biomedical Diagnostic Institute was established in 2006 through funding from Science Foundation Ireland and six industrial partners: Åmic, Analog Devices, Becton Dickinson, Enfer Scientific, Hospira, and Inverness Medical Innovations/Unipath. The institute aims to produce cancer, heart disease and diabetes diagnostic devices. The institute brings together researchers from the Royal College of Surgeons (RCSI), NUIG, and the University College Cork (Dublin City University, 2006).

D.1.2 University College Cork

D.1.2.1 The Biosciences Institute

The Biosciences Institute, located at University College Cork (UCC), was established through SFI and PRTLI funding in 2002. The Institute is partnered with NUIG, RCSI, NUIM, Queens University (Belfast), and UL. The institute promotes interdisciplinary

research collaboration through bringing together researchers from several of the university's biomedical and life sciences departments in the areas of cell, molecular and tissue biology (Biosciences Institute, 2007a: Higher Education Authority, 2006).

The Institute's research programmes include:

- The Research-Neuroscience/Anatomy programme: this is focused on cancer, blindness and neurodegenerative disease such as Parkinson's disease and Alzheimer's disease,
- The Cancer Biology programme: this programme is focused on cancer and degenerative diseases research, in collaborations with the Cork Cancer Research Centre,
- The Cell Signalling Research Programme: this programme is focused on research on the signalling interactions between foetal and maternal tissues in order to understand human reproductive disorders,
- The Research-Food and Health programme: this programme focuses on the roles of food and lifestyle on disease prevention, as well as their therapeutic potential for neurodegenerative disorders (Biosciences Institute, 2007b).

D.1.2.2 The Analytical and Biological Chemistry Research Facility

The Analytical and Biological Chemistry Research Facility was established in 2003 through PRTLI funding totalling €7.7M. The facility draws from the disciplines of Chemistry and Biology. Its activities include measuring dioxin levels in the environment, Testing cell viability with ultra-sensitive Bioassays, and Stress response proteins using proteomic technology (Higher Education Authority, 2006: Analytical and Biological Chemistry Research, 2007).

D.1.2.3 The National Food Biotechnology Centre

The National Food Biotechnology Centre (NFBC) is one of the five Enterprise Ireland Biotechnology Directorate RIs. The centre is a multidisciplinary RI that is focused on the development of services and technology for the food and related industries. The NFBC has played an important role in the formation of two indigenous spin-out bio-firms: Hibergen, and Alimentary Health (BiotechnologyIreland, 2007: University College Cork, 2001).

D.1.2.4 The BIOMERIT Research Centre

The BIOMERIT Research Centre (BRC) was established in 1991. The centre is based in UCC's Microbiology Department and has the aim of developing education and research programmes in innovative biotechnology. Among the centre's facilities are state-of-the-art proteomic and genomic research facilities. The centre's cross-disciplinary research programmes include Immunogenetics and Microbial Pathogenesis, and Environmental Biotechnology (BIOMERIT Research Centre, 2007a, 2007b).

D.1.3 University College Dublin

D.1.3.1 The Conway Institute of Biomolecular and Biomedical Research

The Conway Institute of Biomolecular and Biomedical Research opened in 2003 through funding from the PRTLI programme, the Wellcome Trust, the Health Research Board, SFI and the EU. Its is partnered with TCD, and the RCSI and has established research links with three major centres: Centre for Synthesis and Biology (CSCB) (a University College Dublin-Trinity College Dublin-Royal College of Surgeons, Ireland joint venture), the Centre for Integrative Biology (CIB), and the Dublin Molecular Medicine Centre (DMMC) (Conway Institute, 2004a, 2004b: Higher Education

Authority, 2006).

D.1.3.2 The Centre for Synthesis and Chemical Biology
The Centre for Synthesis and Chemical Biology was established in 2001. The centre is funded through the PRTLI programme, the NDP, and the EU. It is partnered with TCD, and the RCSI. The Centre is one of the three constituent RIs of the Conway Institute. The centre's research programme involves chemical biology research that focuses on the development and use of biological tools for chemistry, biology and medicine, and has developed extensive collaborations with the Dublin Molecular Medicine Centre (DMMC) and the Biopharmaceutical Sciences Network (BSN) at the RCSI (Centre for Synthesis and Chemical Biology, 2007a, 2007b: Higher Education Authority, 2006).

D.1.3.3 National Institute for Bioprocessing Research and Training
The National Institute for Bioprocessing Research and Training (NIBRT) was launched in 2004 in order to providing training and research for the Bioprocessing Industry in Ireland. The NIBRT is located at UCD and is run in collaboration between UCD, TCD, DCU and IT Sligo and has extensive alliances with industry partners. The NIBRT has three main activities: to provide training and education in all aspects of Bioprocessing Technology, to provide research facilities for key aspects of Bioprocessing Technology and Biotechnology, and to provide pilot-plant facilities for scale-up operations **(**Higher Education Authority, 2006; University College Dublin, 2005).

D.1.4 National University of Ireland, Galway (NUIG)
D.1.4.1 The National Centre for Biomedical Engineering Science
The National Centre for Biomedical Engineering Science was established in NUIG in 1999 through PRTLI funding and private donations. The centre combines the skills of engineers, IT specialists, physicians and scientists in order to research cardiovascular disease, reproductive biology, cancer, neurobiology, infectious diseases, biomaterials and biomechanics. The Centre has developed extensive collaborations with its partners UCC, UL, UCD, TCD, GMIT, IT Sligo, Athlone IT (National Centre for Biomedical Engineering Science, 2007a, 2007b: Higher Education Authority, 2006).

D.1.4.2 The National Diagnostics Centre
The National Diagnostics Centre was established in 1987 as one of the five BioResearch Ireland RIs. The Centre is an applied Bio-Sciences Research and Development Centre, its activities are focused in the areas of Immunodiagnostics, Nucleic acid-based diagnostics, and Gene regulation and differential expression (National Diagnostics Centre, 2007).

D.1.4.3 The Martin Ryan Institute
The Martin Ryan Institute was established in 1992 through private donations from the Martin Ryan University Foundation and funding from the EU's STRIDE Operational Programme. The centre's research is focused on marine and freshwater resource studies, in particular in the areas of biology, ecology, physiology and genetics of pelagic and benthic organisms, fisheries biology and economics, physical and chemical oceanography, and marine biotechnology (Martin Ryan Institute, 2007).

D.1.4.4 The Environmental Change Institute
The Environmental Change Institute (ECI) was founded in 2000 through private source and PRTLI funding. The Institute is a member of NUIG's Institute for Environmental Studies. Its research focus is in the areas of Biodiversity, Climate Change, Marine Environment, and Waste (Environmental Change Institute, 2007: The Irish Scientist,

2002).

D.1.5 National University of Ireland, Maynooth (NUIM)

D.1.5.1 The Institute of Immunology

The Institute of Immunology was created in 2003 through a PRTLI investment of €5.5 million. The Institute is engaged in research in the area of immunology, its research themes include Immunity to infectious diseases, Neuroimmunology and inflammation, and Lymphocyte biology (Higher Education Authority, 2006: Institute of Immunology, 2007a, 2007b).

D.1.5.2 The Institute of Bioengineering and Agroecology

The Institute of Bioengineering and Agroecology was established in 2000 through the PRTLI funding programme. The institute brings together six collaborating research laboratories whose research foci include Genetics, Developmental biology, and stress physiology, genetic modification of plants. The Institute's partner institutions are the Dublin Institute of Technology, GMIT, and WIT (Higher Education Authority, 2006: Institute of Bioengineering and Agroecology, 2007).

D.1.6 Trinity College Dublin

D.1.6.1 Trinity Centre for Bio-Engineering

The Trinity Centre for Bio-Engineering was established in 2002 through PRTLI funding. Its partner institute is the National Centre for Biomedical Engineering Science located in NUIG. The centre is focused in biomechanics, specifically relating to skeletal diseases (Tissue Engineering and Mechano-Biology) as well as Pre-clinical testing of implants and medical devices (Higher Education Authority, 2006).

D.1.6.2 The National Pharmaceutical Biotechnology Centre

The National Pharmaceutical Biotechnology Centre was established in 1987 as one of the five BioResearch Ireland RIs. Its research focus is on vaccines, inflammation and cancer, pharmaceuticals, nutriceuticals, bioinformatics and services (BioResearch Ireland, 2001n).

D.1.6.3 Trinity College Institute of Neuroscience and National Neuroscience Network

The Trinity College Institute of Neuroscience and National Neuroscience Network was established in 2002 through PRTLI funding. The Institutes partner institutes include the Trinity College Institute of Neuroscience, UCC, and UCD. The institute is engaged in research in the areas of brain disease, brain damage and brain ageing (Higher Education Authority, 2006).

D.1.6.4 The Sami Nasr Institute for Advanced Materials Science

The Sami Nasr Institute for Advanced Materials Science was established in 2001 through PRTLI funding, it was established in partnership with DCU. The Institute draws together researchers from a wide range of disciplines including physicists, chemists, engineers, clinicians and pharmaceutics. The institute is engaged in research in the areas of supramolecular nanometric magnetic materials, t-lymphatic cell movement on micro-textured surfaces, and Dynamic properties of colloidal suspensions of nano-particles (Higher Education Authority, 2006).

D.1.6.5 The Centre for Research on Adaptive Nanostructures and Nanodevices

The Centre for Research on Adaptive Nanostructures and Nanodevices (CRANN) was established in 2006 through SFI funding. CRANN is a science and engineering technology centre and was created in partnership with UCD and UCC. The centre has

close collaborations with several industry partners including Intel, Hewlett Packard, and many Irish firms. The research topics in the centre are conducted with the centre's researchers and industrial partners across three research areas in the field of nanoscience including Magnetic Structures and Devices, Bottom-Up Fabrication and Testing of Nanoscale Integrated Devices, and Nano-Biology of Cell Surface Interactions (CRANN, 2007a, 2007b).

D.1.6.6 The Institute of Molecular Medicine

The Institute of Molecular Medicine was established in 2003 through PRTLI funding. Its partner institutes are UCD and RCSI. The centre is located on the campus of St James's Hospital, and is dedicated to research into the molecular basis of human disease, in particular cancer and leukaemia, through the sequencing of genes in order to understand the development of human disease (Institute of Molecular Medicine, 2007a, 2007b).

D.1.7 The University of Limerick

D.1.7.1 The Materials and Surface Science Institute

The Materials and Surface Science Institute (MSSI) was established in 1998. It has received €15.7 million in PRTLI funding. The Institute's partners are the Waterford Institute of Technology, NUIG, and UCC. The institute's research is focused on Structural materials, Interfacial science, and Catalysis (Higher Education Authority, 2006).

D.1.7.2 The Centre for Applied Biomedical Engineering Research

The Centre for Applied Biomedical Engineering Research (CABER) was established as part of the University of Limerick's (UL) Department of Mechanical and Aeronautical Engineering in 2004 through funding received from the EU, the NDP, and NUIG's Materials and Surface Science Institute. This multidisciplinary centre brings together researchers in the field of biomedical engineering, and has established collaborations with the Mid-Western Regional Hospital Limerick. The centre's research programmes include cardiovascular biomechanics, tissue engineering, and orthopaedic biomechanics (Centre for Applied Biomedical Engineering Research, 2004).

D.1.7.3 The Centre for Environmental Research

The Centre for Environmental Research was established in 1994, it is a multidisciplinary centre which draws together research experience from chemistry, biochemistry and biology. It has developed alliances with UCC's Environmental Research Institute (Centre for Environmental Research, 2007: University College Cork, 2007).

D.1.8 The Royal College of Surgeons, Ireland

D.1.8.1 The RCSI Research Institute

The RCSI Research Institute is a multi-site research infrastructure that encompasses the entire research activities of the RCSI, it is located in the RCSI and the Education and Research Centre and the Clinical Research Centre at Beaumont Hospital. The Institute integrates basic and clinical research to facilitate the transfer of medical science developments into patient treatments. The institute's core facilities include mass spectrometry, proteomics and genotyping, and bioinformatics. The institute's research programmes include The Programme for Human Genomics, run in partnership with DMMC (RCSI Research Institute, 2007a, 2007b).

D.1.8.2 The Programme for Human Genomics
The Programme for Human Genomics was established in 2003 through one of the largest single PRTLI funding awards. The programme is focused on human disease, in particular in the areas of cancer, cardiovascular disease, inflammation and therapeutics. The Programme's partner institutions include TCD, and UCD (Higher Education Authority, 2006).

D.1.8.3 The Biopharmaceutical Sciences Network
The Biopharmaceutical Sciences Network was created in 1999 through PRTLI funding. It is located at the RCSI's Clinical Research Centre at Beaumont Hospital, and is engaged in collaborative programmes with RCSI, TCD, UCC, and NUIM. The hospital based centre is engaged in evaluating innovative therapies in order to improve the quality of patient (Higher Education Authority, 2006).

D.1.8.4 The Clinical Research Centre
The Clinical Research Centre was established in 2000, partly through PRTLI funding. It is located at the RCSI's research teaching facility at Beaumont Hospital. The Centre provides state of the art research equipment and facilities to academic and industrial partnerships in order to develop new therapies through clinical trials and basic research (Clinical Research Centre. 2007: The Irish Scientist, 2001).

D.1.8.5 Biopharmaceutical Sciences Network
The Biopharmaceutical Sciences Network (BSN) was established in 2000 through PRTLI funding. The BSN is a collaboration between the RCSI, TCD, UCC and NUIM. The BSN developed from a RCSI pharmacogenics programme, it now includes a series of research cores:

- The National Transgenic Centre: located in TCD, this is Irelands first transgenic facility,
- The National Probiotics Centre: based in UCC, this centre's research is focused on probiotic bacteria in order to develop treatments for inflammatory bowel diseases and infections,
- The Centre of Advanced Drug Delivery: this centre researches new drug delivery methods using gene therapy constructs,
- The Virtual Institute of Bioinformatics in Éire: this is a cross-institution institute between the RCSI, NUIM, TCD, and UCD. The institute combines bioinformatic research activities of the host universities (VIBE, 2007, Royal college of Surgeons, Ireland, 2007, The Irish Scientist, 2000).

D.2 UNIVERSITY AFFILIATED RESEARCH INSTITUTES

D.2.1 Dublin Molecular Medicine Centre

The Dublin Molecular Medicine Centre (DMMC) was established in 2002 through funding received from the PRTLI programme and the NDP. The centre is an independent partnership between RCSI's Programme for Human Genomics, the Durkan Institute at TCD, UCD's Conway Institute, and six Dublin based hospitals. The DMMC's activities are focused on four biomedical areas: Cancer, Infection, Inflammation and Immunity, Neuroscience, and Vascular biology (Higher Education Authority, 2006).

The centre conducts five research programmes:

- The Programme for Human Genomics: funded by the HEA, this is a cross-institutional and translational research programme between the DMMC and researchers in the Royal College of Surgeons, Ireland and Trinity College Dublin (TCD). As the DMMC's activities are based around medicine and pharmaceutical-related research, areas in which genomic research (as stated in chapter 1) could potentially have enormous impacts, this programme is expected to develop into a significant research area in the coming years,
- The Prostate Cancer Research Consortium: this consortium brings together researchers from the partner universities and hospitals in research to identify disease biomarkers for improved detection and prognosis,
- The All Ireland Cystic Fibrosis Research Consortium: this consortium is engaged in collaborative research between Irish and US researchers in order to develop Cystic Fibrosis pattern overviews and to develop improved screening services, and
- The Breast Cancer Research Consortium: this consortium involves collaborations between the partner institutions researchers to establish a common research infrastructure to facilitated the establishment of a biobank of serum and tissue material drawn from a patient population (Dublin Molecular Medicine Centre, 2007a).

The DMMC is hosts the Gene Archive of Ireland. Established between the DMMC and the RCSI through PRTLI funding, this aims to assist in the development, diagnosis and treatment of diseases at partner institutions (Dublin Molecular Medicine Centre, 2007b).

D.2.3 Centres for Science, Engineering & Technology

SFI established the Centres for Science, Engineering & Technology (CSETs) university-industry partnerships in 2003. The CSET centres are designed to assist the development of alliances between academic (scientific and engineering) researchers in partnerships with industry in order to facilitate the development of new and existing Irish technology-based companies. CSET grants are competitive in nature and range from €1 to €5 million per year for up to ten years.

There are eight CSET centres biotechnology/biotechnology-related CSET centres, the following four are engaged in biotechnology/biotechnology-related activities:

- The Alimentary Pharmabiotic Centre (APC): APC was established in 2003 and is based at UCC. The APC draws together scientists and clinicians from several UCC faculties including medicine, science, food science and nutrition, and is partnered with Teagasc, Alimentary Health, Procter & Gamble Co and GlaxoSmithKline. The APC's research activities are in the areas of intestinal bacterial influences on health, developing therapies for gastrointestinal diseases such as gastroenteritis and Crohn's disease, and exploring commercial opportunities in both the pharma and functional food sector.
- The Centre for Research on Adaptive Nanostructure & Nanodevice (CRANN): CRANN is based at TCD, it was established in 2004. Its partner universities are UCC and UCD, its principal industry partners are Intel Ireland and Hewlett-Packard. The centre brings together researchers from physics, chemistry, and biology in the area of nanoscience to develop new products and processes in microelectronics and drug delivery systems.
- Regenerative Medicine Institute (REMEDI): REMEDI is located in NUIG and was established in 2003. The centre is engaged in research focused at developing techniques for tissues and organs repair. The Centre's industrial partners are

Medtronic Vascular (Galway), and Charles rivers Laboratories.

- Biomedical Diagnostic Institute (BDI): The BDI was established in 2005, it is primarily located in DCU. It is partnered with the National Centre for Sensor Research in DCU, the National Centre for Biomedical Engineering Science at NUIG, the RCSI, and the Tyndall National Institute at UCC. The Institute is engaged in research that is focused on developing biomedical diagnostic devices for a wide range of chronic diseases including cancer, and cardiovascular diseases. The BDI's industrial partners include Analog Devices, Inverness Medical Innovations, and Enfer Technologies (Alimentary Pharmabiotic Centre, 2007: Forfás, 2004: The Irish Scientist, 2003: University College Cork, 2003: Science foundation Ireland, 2002, 2007).

D.2.3 Teagasc's Rresearch Institutes

Teagasc, the Irish Agriculture and Food Development Authority, has 9 RIs (Centre of Excellence), the following centres are engaged in biotechnology or biotechnology-related research:

- The Moorepark Dairy Production Research Centre and Food Research Centre: The Moorepark Centres are engaged in research and the provision of technological services to the Irish dairy processing and food ingredients sectors, as well as research in dairy processing, food ingredients, and nutritional foods. The Food Research Centre is engaged in collaborative research with UCC's alimentary pharmabiotic research centre,
- The Kinsealy Research Centre: The Kinsealy Centre is engaged in research and technical development for the Irish horticultural industry, providing relevant technological data to optimise the competitiveness of the sector. The Centre's research includes biotechnology, forestry, protected food and vegetable crop programmes,
- The Grange Research Centre: The Grange Centre is engaged in research relating to beef production systems, and houses the Blood Laboratory which provides a national blood service to farmers,
- The Oak Park Research Centre: The Oak Park Centre is focused in arable crop research. Teagasc's Plant Biotechnology Unit is located in the Centre (where the first Irish trials of genetically modified crop trials were carried out in 1997 in collaboration with Monsanto), and
- The Johnstown Castle Environment Research Centre: The Johnstown Castle centre is engaged in research on soils and the environment, it is home to the Teagasc Analytical Services Laboratory for soil, herbage, water and general agricultural materials (Teagasc, 1999, 2005a, 2005b, 2006).

Two minor RIs (Belclare and Athenry) conduct biotechnology research as part of the Teagasc Beef Research Programme. This programme aims to develop "...the base of expertise and information in generic technologies to assist the Irish food industry to achieve...product and process innovations" (Teagasc, 2005, 2006).

D.3 INSTITUTE OF TECHNOLOGY RESEARCH INSTITUTES

D.3.1 Athlone Institute of Technology

D.3.1.1 Centre for Biopolymer and Biomolecular Research

The Centre for Biopolymer and Biomolecular Research was established in 2000 through PRTLI funding. Its partner institutes are NUIG, and the University of Ulster, Colrane. The centre's research is focused on the areas of biopolymers and biomolecular research (Higher Education Authority, 2006).

D.3.2 Dublin Institute of Technology

D.3.2.1 The Facility for Optical Characterisation and Spectroscopy

The Facility for Optical Characterisation and Spectroscopy was established in 2002 through PRTLI funding totaling €10.4M. The Facility is formed by 6 interdisciplinary research groups in physics, chemistry and materials science whose research is focused on Pharmaceuticals, Urban Air Pollution, Radiation, Optical Sensing, Optoelectronics, and Nanotechnology (Higher Education Authority, 2006).

D.4 RESEARCH AND TEACHING HOSPITALS

D.4.1 Beaumont Hospital

Beaumont Hospital opened in 1987, it is the National Referral Centre for Neurosciences and Renal Transplantation. It has developed research alliances with the RCSI in relation to neurosciences research. Located at Beaumont Hospital are the RCSI Medical School. This is overseen by the Department of Medicine in Beaumont Hospital, clinical teaching for approximately two thirds of third and final year medical students of the RSCI Department of Surgery are conducted at the school, with research being conducted in the areas of cancer research (in collaboration with DCU's National Institute for Cellular Biology) cardiology, respiratory medicine, gastroenterology, nephrology and endocrinology (Beaumont Hospital, 2000a, 200b: Irish Press Releases, 2007; National Institute for Cellular Biology, 2007; The Irish Scientist, 2001).

D.4.2 Blackrock Clinic

Established in 1984, Blackrock Clinic's facilities include a coronary care unit, an intensive care unit, and two Cardiac Cathterisation Laboratories. The Clinic has developed education programmes the RCSI and UCD, and is engaged in molecular cancer research with the National Institute for Cellular Biotechnology (Blackrock Clinic, 2007; Molecular Cancer, 2006).

D.4.3 Mater Misericordiae University Hospital

The Mater Misericordiae University Hospital was established in 1861. The hospital has two national specialities, cardiothoracic surgery (including transplantation) and spinal injuries, while also providing cardiology, renal services, general and vascular surgery, urology and orthopaedics services. The Mater houses a Medical School (affiliated to UCD and the RCSI), a Centre for Nurse Education in partnership with the School of Nursing UCD, a School of Physiotherapy affiliated to UCD, an Institute of Radiological Science, and the Catherine McAuley Education and Research Centre (a collaborative RI formed in alliance with UCD, with linkages with the genome resource unit of the Dublin Molecular Medicine Centre). The hospital has also developed collaborative research programmes in cancer research with UCD's Conway Institute (Dublin Molecular Medicine Centre, 2004; Mater Misericordiae University Hospital, 2004: Mater Private hospital, 2007a, 2007b).

D.4.4 St. James's Hospital

St. James's Hospital was established in 1971 through the amalgamation of smaller voluntary hospitals in Dublin. Located in St. James's Hospital is a teaching hospital for TCD and a Teaching Centre, opened in 1994, that incorporates the clinical departments of the medical school, the unit for dietetics and nutrition, the nursing school, the postgraduate centre and the library of the Faculty of Health Sciences (St. James's Hospital, 2007a).

The St. James Biochemistry Department is the national centre for investigation and

diagnosis of Porphyria (enzyme disorders) and provides an extensive range of endocrinology assays to a variety of Irish hospitals including the Meath Hospital, the Adelaide Hospital and the National Children's Hospital (St. James's Hospital, 2007b).

Located at St. James's are a Bio-incubator and clinical trial facilities. The bioincubator was launched in 2006 by the hospital and EI in order to assist the formation of laboratory and serviced biotechnology companies. Two EI supported firms, Opsona Therapeutics and Cellix, are located at the incubator. The clinical trial facilities were opened in 2002 by the Dublin Molecular Medicine Centre (DMMC), in collaboration with the Health Research Board (HRB) and the Wellcome Trust (Department of Enterprise, Trade and Employment, 2006).

D.4.4 St Patrick's Hospital

St Patrick's Hospital has developed a wide ranging clinical research programme with the Academic Psychiatric Unit at St James's Hospital. The Depression Research Unit is engaged in a wide variety of research themes including diagnostic sensitivity and therapeutic effectiveness research in Alzheimer's disease (St Patrick's Hospital, 2004).

D.4.5 St. Vincent's University Hospital

St Vincent's University Hospital was originally opened in 1934, since 1999 it has acted as a major academic teaching hospital affiliated to University College Dublin. St. Vincent's Education and Research Centre is one of the main Biomedical RIs in Ireland. The centre's research programmes complement the clinical and treatments conducted in the Hospital, these include the National Liver Transplant Programme, National Early Arthritis Clinic, part of the National Breast Screening Programme, and a clinical centre for Hepatitis C. The hospital's Centre for Colorectal Disease was established to provide clinical care for the hospital's patients, it is engaged in collaborative research programmes with the Biotechnology Centre of UCD, the RCSI and UCC (St. Vincent's University Hospital, 2007).

In 2007, St Vincent's formed, in collaboration with the Mater University Hospital and UCD's School of Medicine and Medical Science, Ireland's first academic medical clinical care centre; Dublin Academic Health Care Centre. This centre is engaged in clinical care, teaching and research, aims to facilitate rapid and effective transfer of research ideas into clinical practice (University college Dublin, 2007)

D.4.6 Adelaide and Meath Hospital (incorporating the National Children's Hospital) in Tallaght

The Adelaide and Meath Hospital is one of the main general teaching hospitals of TCD. The TCD Centre for Health Sciences at Tallaght houses the academic Departments of Paediatrics, academic clinical units of Clinical Medicine, Surgery, Gynaecology, Psychiatry, the hospital library and College of Nursing, and research laboratories (Adelaide and Meath Hospital, 2007).

D.4.7 Temple Street Children's University Hospital

Founded in 1872, the Temple Street Children's University Hospital is an Acute Paediatric Hospital. The Hospital is home to a variety of National Centres, including the National Centre for Inherited Metabolic Disorders, the National Screening Laboratory, and the National Centre for Paediatric Ophthalmology. The Hospital has teaching alliances with the RCSI and UCD in the areas of Radiography, Physiotherapy, Psychology, Psychiatric and Medical Social Work (Children's University Hospital, 2007).

D.4.8 Merlin Park Regional Hospital

Merlin Park Regional Hospital is a member of the Galway Regional Hospitals Group with Galway University Hospital, as such it has extensive alliances with the NUIG. The hospital is a regional centre for a wide range of specialties including Cardiology, Respiratory Medicine, Plastic Surgery, Vascular Surgery, and Neurology. The hospital is engaged in biotechnology-related research with NUIG's REMEDI Clinical Research Facility (Western Health Board, 2007b).

D.4.9 Galway University Hospital

Galway University Hospital is located adjacent to NUIG, it is a specialist hospital and the main teaching hospital of NUIG's Medical School. The Hospital includes NUIG's Clinical Science Institute which contains the Hospital's laboratories. The hospital has developed extensive collaborations with NUIG's REMEDI clinical research facility in the areas of genomic based molecular research, cancer and regenerative medicine research (REMEDI, 2007; Western Health Board, 2007a).

D.4.10 Cork University Hospital

Cork University Hospital was purpose built in 1979, it houses Departments of Medicine, Surgery, Obstetrics/ Gynaecology, Paediatrics, Pathology and Psychiatry. It is the principal teaching hospital attached to UCC. The hospital is part of a city-wide group of hospitals which includes, St. Finbarr's Hospital, Erinville Hospital and St. Mary's Orthopaedic Hospital (Southern Health Board, 2006).

D.4.11 Mercy Hospital

The Mercy Hospital plays an active part in the undergraduate and postgraduate medical and nursing teaching programmes of University College Cork and has a number of research programmes including the Cork Cancer Research Charity Laboratory (Mercy Hospital, 2004).

APPENDIX B:
LETTERS AND OTHER CONTACTS WITH TARGET BIOTECHNOLOGY FIRMS

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

Dear Mr. Doe

I am currently conducting a study of networks and interlinkages between firms in the Irish biotechnology industry. International studies have highlighted the importance of such networks and linkages in the development of the industry. This study, which is sponsored by the National Institute for Regional and Spatial Analysis (NIRSA), seeks to optimize the development of the biotechnology industry in Ireland through enhancing the formation and functioning of networks among the sector's actors.

As part of this study, I will be sending you, in the next few days, a questionnaire survey form relating to your own firm's networking arrangements. I would be very grateful if you would take the time to complete this survey which will assist in the formulation of effective policies for the development of the Irish biotechnology industry.

Thank you for your time and consideration. I look forward to receiving your assistance in the completion of this study.

Yours sincerely,

_____

John O'Byrne
Doctoral Research Fellow, NIRSA

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National University of Maynooth
Co. Kildare, Ireland

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

Biotechnology Company
Ireland

Dear Mr. Doe

In the last few days you should have received a letter from me requesting your assistance in completing a questionnaire survey relating to networks in the Irish biotechnology industry. This study is sponsored by the National Institute for Regional and Spatial Analysis (NIRSA), and is primarily aimed at optimizing the development of the biotechnology industry through enhancing the formation and functioning of networks among the sector's actors. As you will know, biotechnology has been identified by the Irish government as playing a key role in the future development of the Irish economy.

The survey is concerned with collaborative or networking arrangements that may exist between your firm and other actors in the biotech industry. Such arrangements are formed in order to achieve shared objectives or benefits and include (for example) joint marketing or the exchange of skills, equipment, and information. The survey mainly consists of a series of open-ended questions that allow you to elaborate on your firm's specific experiences in forming networks with sector actors in the Irish biotechnology industry.

I would be very grateful if you could take the time to complete the enclosed survey form. The successful completion of this study is dependent on you completing this survey and sharing your experiences of working within the Irish biotechnology sector. Completion of the survey should take no more than 10 minutes. Your answers will be kept **completely confidential** and the survey results will be released only in summary form so no individual's answers can be identified.

If you have any questions or comments about this study, I would be happy to talk with you. You can contact me at the addresses or number on the letterhead. A summary of the survey findings will be sent to all participating firms.

Thank you very much for helping us with this important study.

Yours sincerely,

_____

John O'Byrne
Research Fellow, NIRSA

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E Mail: john.p.obyrne@nuim.ie

National University of Maynooth
Co. Kildare, Ireland

3rd August, 2004

NUI MAYNOOTH

Last month a survey form on networks in the Irish biotechnology sector was posted to you.

If you have already completed and returned the survey to me, please accept my sincere thanks. If not, could you please do so today. I am especially grateful for your help because it is only through you, sharing your experiences of networks among Irish biotechnology firms that this study can be successfully completed.

If you did not receive a survey form, or it was misplaced, please call me at 01-7086208 or e-mail me at john.p.obyrne@may.ie and I will get another one in the post to you today.

An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

John O'Byrne
Research Fellow
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An Chomhairle um Thaighde sna Dána agus sna hEolaíochtaí Sóisialta
Irish Research Council for the Humanities and Social Sciences
IRCHSS

NIRSA
National Institute For Regional And Spatial Analysis

Dear Mr. Doe

I am writing to you to thank you for completing my questionnaire survey form (relating to your own firm's networking arrangements) which I sent out to you over a month ago. I gratefully appreciate your response.

Please note that your answers will be kept **completely confidential** and the survey results will be released only in summary form so no individual's answers can be identified.

If you have any questions or comments about this study, I would be happy to talk with you. A summary of the survey findings will be sent to all participating firms.

Thank you very much for helping with this important study.

Yours sincerely,

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Dear Mr. Doe

In the last month or so, you should have received a letter from me requesting your assistance in completing a questionnaire survey relating to networks in the Irish biotechnology industry. This study is sponsored by the National Institute for Regional and Spatial Analysis (NIRSA), and is primarily aimed at optimizing the development of the biotechnology industry through enhancing the formation and functioning of networks among the sector's actors. As you will know, biotechnology has been identified by the Irish government as playing a key role in the future development of the Irish economy.

The survey is concerned with collaborative or networking arrangements that may exist between your firm and other actors in the biotech industry. Such arrangements are formed in order to achieve shared objectives or benefits and include (for example) joint marketing or the exchange of skills, equipment, and information. The survey mainly consists of a series of open-ended questions that allow you to elaborate on your firm's specific experiences in forming networks with sector actors in the Irish biotechnology industry.

I would be very grateful if you could take the time to complete the enclosed survey form. The successful completion of this study is dependent on you completing this survey and sharing your experiences of working within the Irish biotechnology sector. Completion of the survey should take no more than 10 minutes. Your answers will be kept completely confidential and the survey results will be released only in summary form so no individual's answers can be identified.

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Thank you very much for helping us with this important study.

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National Institute For Regional And Spatial Analysis

Dear Mr. Doe,

My name is John O'Byrne, I am currently engaged in research for my PhD thesis entitled "Networks and the development of the Irish biotechnology sector" at the NUI, Maynooth.
My study, which is sponsored by the Irish Research Council for the Humanities and the Social Sciences (IRCHSS) and the National Institute for Regional and Spatial Analysis (NIRSA), seeks to optimise the development of the biotechnology industry in Ireland through enhancing the formation and functioning of networks among the sector's actors.
I am presently conducting a study of networks and interlinkages between universities and the Irish biotechnology industry, and as such, I would like to interview key university staff members who are involved in collaborations/alliances (research based, or otherwise) with biotechnology firms, corporations (e.g. pharmaceutical companies) and other universities.
I am curious if it would be possible for me to set up an interview with you to explore your experiences in facilitating University/biotechnology firm alliances/collaborations?
Please note that any information received during any correspondence will be treated with the utmost confidentiality.

Yours sincerely,
John O'Byrne

Doctoral Research Fellow

Irish Research Council for the Humanities and the Social Sciences
http://www.irchss.ie/

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Co. Kildare, Ireland

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I am presently conducting a study of networks and interlinkages that exist between indigenous biotechnology companies and the Irish biotechnology industry.
As such, I would like to interview key firm members who are involved in collaborations/alliances (research based, or otherwise) with university based researchers, corporations (e.g. pharmaceutical companies) and other indigenous biotechnology firms.
I am curious if it would be possible for me to set up an interview with you to explore your experiences in relation to your firms networking activities?
Please note that any information received during any correspondence will be treated with the utmost confidentiality.

Yours sincerely,
John O'Byrne

Doctoral Research Fellow

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National Institute For Regional And Spatial Analysis

Dear Mr. Doe,

My name is John O'Byrne, I am currently engaged in research for my PhD thesis entitled "Networks and the development of the Irish biotechnology sector". My study, which is sponsored by the Irish Research Council for the Humanities and the Social Sciences (IRCHSS) and the National Institute for Regional and Spatial Analysis (NIRSA), seeks to optimise the development of the biotechnology industry in Ireland through enhancing the formation and functioning of networks among the sector's actors.
I am presently conducting a detailed study of existing networks and interlinkages between all sectoral actors in the domestic biotechnology sector, and as such, I would like to interview key staff members of agencies that are involved in the sector.
I am curious if it would be possible for me to set up an interview in order to explore your experiences/views/opinions in relation to the domestic biotechnology sector?
Please note that any information received during any correspondence will be treated with the utmost confidentiality.

Yours sincerely,
John O'Byrne

Doctoral Research Fellow

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APPENDIX C:
BIOTECHNOLOGY/BIOTECHNOLOGY-RELATED DEPARTMENTS IN IRISH UNIVERSITIES

This appendix details and discusses the various biotechnology/biotechnology-related departmental and educational activities conducted by Irish university biotechnology/biotechnology-related departments and faculties.

There are eight Universities in Ireland:

- Dublin City University (DCU)
- University College Cork (UCC)
- University College Dublin (UCD)
- National University of Ireland Galway (NUIG)
- National University of Ireland Maynooth (NUI, Maynooth)
- Trinity College Dublin (TCD)
- the University of Limerick (UL), and
- the Royal College of Surgeons, Ireland

C.1 DUBLIN CITY UNIVERSITY

Founded in 1980 as a technical college, Dublin City University (DCU) was awarded university status in 1989. DCU was the first Irish University to establish an undergraduate degree in Biotechnology in the mid 1980s (Dublin City University, 2005).

C.1.1 DCU Faculties

C.1.1.1 Faculty of Science and Health

The six schools of DCU's Faculty of Science and Health's teaching and research activities are inter-disciplinary focused. Among the teaching aspect of the various faculty school programmes are physical and biological sciences (Dublin City University, 2007a).

C.1.1.1.1 School of Biotechnology

DCU's School of Biotechnology incorporates teaching and research facilities in a single departmental unit for Process Engineers, Biochemists, Microbiologists, Geneticists and Pharmacologists. The school has established basic and applied research collaborative links with national and international research laboratories and has developed close alliances with DCU based research centres (discussed in further detail in Appendix D) such as the National Institute for Cellular Biotechnology (NICB) and the National Centre for Sensor Research (NCSR) (Dublin City University, 2005).

The School's undergraduate programme includes four year B.Sc. degrees in Biotechnology, Environmental Science & Health, and Genetics and Cell Biology. The School's postgraduate degree programmes include a M.Sc. in Bioinformatics, and a GDip/MSc in Biomedical Diagnostics (Dublin City University, 2007b, 2007c, 2007d, 2007e, 2007f).

C.1.1.1.2 School of Chemical Sciences

The School of Chemical Sciences research activities include environmental and analytical chemistry, combinatorial synthesis, nanotechnology, photochemistry and spectroscopy research programmes. Close research collaborations have developed between the school and the NICB and the NCSR. The School's teaching programmes

include B.Sc. degrees in Analytical Science, Chemical and Pharmaceutical Sciences (Dublin City University, 2007g, 2007h, 2007i).

C.2 UNIVERSITY COLLEGE CORK

University College Cork (UCC) was founded in 1845 and is the second largest university in Ireland (University College Cork, 2007).

C.2.1 UCC Faculties

UCC's College of Science, Engineering and Food Science comprises of the Faculties of Science, Engineering, and Food Science and Technology (University College Cork, 2006a).

C.2.1.1 The Faculty of Science

UCC's Faculty of Science includes the Departments of Biochemistry, Chemistry, Microbiology, Zoology, Ecology, and Plant Science (University College Cork, 2007).

C.2.1.1.1 The Department of Biochemistry

Established in 1945, the Department of Biochemistry is engaged in molecular and cellular education, training and research. The Department of Biochemistry's undergraduate programmes include a four year B.Sc. in Biochemistry, this degree focuses on the biological and chemical sciences. The degree involves courses on Structural Biochemistry, Membrane Biochemistry, Cell Signalling, Biochemical Immunology, Principles of Medical Genetics, and Bioinformatics. The Department it is also involved in the Biomedical Sciences degree, the BSc in Genetics, the preclinical years of the medical degree (MB, BCh, BAO), dental degree (BDS) courses in the medical foundation year, and the BSc in chemistry of pharmaceutical compounds. The Department's postgraduate degree programmes include Higher Diploma in Applied Science (Biotechnology), and a M.Sc. degree in Applied Science (Biotechnology) (University College Cork, 2003a, 2006b)

C.2.1.1.2 The Department of Microbiology

The Department of Microbiology is a member of two UCC Faculties, the faculty of Science and Food Science and Technology and the Faculty of Medicine. The Department has established close research and teaching ties with UCC departments, including the Department of Food Science and Technology, the Department of Medicine. Extensive collaborations have developed with Teagasc's Dairy Products Centre in Moorepark, Fermoy. The department's research programmes include topics in Genomics and Molecular Biology (University College Cork, 2005).

The Department's undergraduate programme includes a B.Sc. in Biology that has six possible specialisations: Microbiology, Plant and Microbial Biotechnology, Biomedical Sciences, Food Sciences, Food Technology, and Genetics. The Department's postgraduate degree programmes include a research based M.Sc. degree. This is based upon a research project completed under the supervision of a faculty member (University College Cork, 2005).

C.2.1.1.3 The Department of Zoology, Ecology, and Plant Science

The Department of Zoology, Ecology, and Plant Science (ZEPS) was formed in 2002 with the amalgamation of UCC's Departments of Zoology and Animal Ecology, and Plant Science. The Department's research activities are in the areas of marine, terrestrial and freshwater animal/plant ecology, environmental plant biotechnology, and population

genetics (University College Cork, 2003b).

The Department's undergraduate degree programmes include B.Sc. degrees in Zoology, Applied Ecology, and Environmental Plant Biotechnology. The Department's postgraduate degree programmes include s a two year M.Sc. in Ecosystem Conservation and Landscape Management (University College Cork, 2007, 2006c).

C.2.1.2 The Faculty of Food Science and Technology

The Faculty of Food Science and Technology's activities are focuses on the areas of Dairy and Food Science education and research, including Food Biotechnology. There are 5 Departments in the Faculty including the Departments of Food, Business and Development, Microbiology (discussed above), Food and Nutritional Science, and Process and Chemical Engineering. The Faculty has developed close connections with the National Food Biotechnology Centre (NFBC) (University College Cork, 2006a).

C.2.1.2.1 The Department of Food, Business and Development

The Department is focused on research relating to the agri-food industry, including developing current agricultural practices, to food processing. The research activities of the Department are focused on three general topics, Food Business, co-operative Business, and Rural Development.

The Department's undergraduate programmes include a 2 year B.Sc. in Food Business. This degree combines Food Business and Food Science and Technology courses. Business and marketing skills are combined with knowledge of food products and processes. The Department's postgraduate degree programmes include a range of postgraduate courses and research programmes are offered by the department. Ph.D. and MSc research programmes in Food Chemistry, Food Economics, Food Engineering, Food Technology, Microbiology and Nutrition are available (University College Cork, 2007d, 2007e).

C.2.1.2.2 The Department of Physiology

The Department of Physiology brings together academics from the fields of physiology, pharmacology, biochemistry, molecular biology and clinical research. The Department's research involves programmes in the fields of Cell, Molecular and Integrative Physiology. Collaborative research projects are conducted with researchers from the Departments of Microbiology and Anatomy, and the Biosciences Research Institute (University College Cork, 2007f, 2007g).

C.3 UNIVERSITY COLLEGE DUBLIN

University College Dublin (UCD) was originally established in 1854. UCD is Ireland's largest university with 5 Colleges and 35 Schools. The University's biotechnology and biotechnology-related research is conducted in the Departments of Medicine, Veterinary Medicine and Agriculture as well the Department of Biochemistry, Industrial Microbiology, Botany, Zoology, Microbiology and Pharmacology, yet the main activity is carried out in the faculty of Science where research efforts focus on microbiology, molecular genetics, toxicology, immunology, drug design, biodiversity, industrial microbiology, pharmacology and zoology (Burke at al., 2003).

C.3.1 College of Engineering, Mathematical and Physical Sciences

There are 7 schools in the College of Engineering, Mathematical and Physical Sciences, including the School of Chemical and Bioprocess Engineering (University College

Dublin, 2007a).

C.3.1.1 The UCD School of Chemical and Bioprocess Engineering
The School of Chemical and Bioprocess Engineering is engaged in research in the areas of Bioprocess engineering, Cell biology, Biofilm Engineering, and Animal Cell Culture Technology. The School's teaching programmes include a 4 year B.E. in Chemical Engineering or Bioprocess Engineering and taught and research MEngSc degrees (University College Dublin, 2006, 2007b, 2007c).

C.3.2 The College of Life Sciences
The College of Life Science comprises eight scientific schools, and the UCD Veterinary Hospital (University College Dublin, 2007d).

C.3.2.1 School of Agriculture, Food Science and Veterinary Medicine
The school engages in research and teaching programmes focused on animal health and welfare, human health, food systems and agriculture. The School's undergraduate degree programmes include B.Sc. degrees in Food Science, Food & Agri-Business Management, Agri-Environmental Sciences, Animal & Crop Production, Animal Science, and in Engineering Technology. The School's postgraduate degree include research M.Sc. degrees in Science, Science (Agriculture), Agricultural Science, Animal Science, Engineering Science, and in Veterinary Medicine. The School also offers taught M.Sc. degrees in Engineering Science: Food Engineering, and Engineering Technology (University College Dublin, 2007e, 2007f, 2007g, 2007h).

C.3.2.2 UCD School of Biology and Environmental Science
The school engages in teaching and research in the areas of modern biology and environmental science, these include programmes in botany, cell and molecular biology, environmental science, genetics, and zoology. The school's research programmes cover a wide range of areas: general zoology, animal behaviour, biodiversity, bioremediation, cell biology, developmental biology, genetics, and marine fisheries (University College Dublin, 2007i).

C.3.2.3 UCD School of Biomolecular and Biomedical Science
The School brings together academics different disciplines including Biochemistry, Microbiology, Pharmacology and Physiology. The school's research and teaching programmes are focused biological systems at molecular, cellular and whole organism levels. The school is part of the Conway Institute of Biomolecular and Biomedical Research (University College Dublin, 2007j).

The School's undergraduate programmes include B.Sc. (Honours) and B.Sc. (General) degrees in Biochemistry, Microbiology, Pharmacology and Physiology. B.Sc. (Joint Honours) programmes are also available to prospective students, which can be combined with degrees in other disciplines including Chemistry and Molecular Genetics (University College Dublin, 2007k).

C.3.2.4 UCD School of Chemistry and Chemical Biology
The School is home to 24 research groups with interests spanning a wide range of chemical sciences. The School opened the Centre for Synthesis and Chemical Biology (CSCB) in 2005. The School of Chemistry and Chemical Biology's teaching programmes include a 4 year B.Sc. in Medicinal Chemistry & Chemical Biology that was introduced in 2007 (University College Dublin, 2007l, 2007m).

C.3.2.5 UCD School of Medicine and Medical Science

The School has developed clinical research programs in six Dublin partner hospitals:

- the Mater Misericordiae University Hospital;
- St. Vincent's University Hospital;
- the National Maternity Hospital;
- the Coombe Women's Hospital;
- Our Lady's Hospital for Sick Children; and
- the Children's University Hospital at Temple Street.

The school's research programmes range from fundamental biology through translational research to population and clinical research. The school has extensive collaborations with the Conway Institute of Biomolecular and Biomedical Sciences and the Dublin Molecular Medicine Centre. The School's teaching programmes include a B.Sc. in Biomedical Health and Life Sciences as well as taught and research postgraduate level M.Sc. degrees (University College Dublin, 2007n, 2007o).

C.4 NATIONAL UNIVERSITY OF IRELAND, GALWAY

The National University of Ireland at Galway (NUIG) was originally founded in 1845, and became one of the National Universities of Ireland in 1997 (National University of Ireland, Galway, 2007a).

C.4.1 The Faculty of Medicine, Nursing, and Health Sciences

C.4.1.1 The Department of Bacteriology

The Department hosts the National Salmonella Reference Laboratory for Ireland, while its research activities include Antimicrobial Resistance in Human and Animal Pathogens. The department is closely associated with the Department of Medical Microbiology at NUIG's University College Hospital. The Department of Bacteriology's Bacteriology course begins in the final term of the Third Medical year. The Department also runs a Mechanisms of Disease course jointly with the Department of Pathology (National University of Ireland, Galway, 2007b, 2007c).

C.4.2 The Faculty of Science

The Faculty of Science's department include the Department of Biochemistry, Chemistry, Microbiology, and Pharmaceutical and Therapeutics. The faculty of science offers two types of B.Sc. degrees, the undenominated programme (a three year degree that has a general focus to allow students to identify the area they are most interested in) and the denominated programme (this has a specific focus and is four years long) (National University of Ireland, Galway, 2003, 2007d).

C.4.2.1 The Department of Biochemistry

The Department of Biochemistry was established in 1963. The department's activities involve activities in the areas of genetics, immunology, cell biology and structural biology. The Department's undergraduate programmes include a B.Sc. in Biochemistry. The Department of Biochemistry, in collaboration with the Departments of Microbiology and Medicine, offers a B.Sc. in Biotechnology. The B.Sc. in Biotechnology is a four year degree in which students specialise in one of the following subject areas: Anatomy, Physiology or Biochemistry. The degree also includes an annual ICT module, the aim being to produce graduates with the necessary skills needed in industry (National University of Ireland, Galway, 2007e, 2007f).

C.4.2.2 The Department of Chemistry
The Department of Chemistry was founded in 1849, its research activities include Environmental Chemistry, Chemical Synthesis, and Bioanalytical Chemistry. The Department offers a four year B.Sc. Programme, and a H.Dip. in Analytical Chemistry and Biochemistry (National University of Ireland, Galway, 2007g, 2007h).

C.4.2.3 The Department of Botany
The Department of Botany offers Botany B.Sc. degrees at general and honours level. The first year of the degree entails an extensive course in basic Biology (no prior knowledge of biology is necessary for students). The second and third years of the degree become more specialized in their focus. Only in the fourth year (when a student has qualified to complete an honours degree) is Botany studied exclusively. The Botany Department also contributes extensively to the Denominated B.Sc. Degrees in Marine and Environmental Science (National University of Ireland, Galway, 2007i).

C.4.2.4 The Department of Microbiology
The Department of Microbiology was established in 1965. The department's research focuses are in the areas of biotechnology, environmental microbiology, aquaculture, marine sciences, genetics and bacterial pathogenesis (National University of Ireland, Galway, 2007j).

C.4.2.5 The Department of Pharmacology
The Department was formed in 1974, its research activities focus on the central nervous system, in particular the mechanism of action of antidepressants and drugs of abuse. The Department's undergraduate programmes include courses on Medicine, and B.Sc. degrees in Biotechnology, Biomedical Science and Nursing (National University of Ireland, Galway, 2007k).

C.5 NATIONAL UNIVERSITY OF IRELAND, MAYNOOTH
The National University of Ireland at Maynooth (NUIM) was established as a university in 1997 (National University of Maynooth, 2007a).

C.5.1 The Faculty of Science & Engineering
C.5.1.1 The Department of Biology
Established in 1970, the Department of Biology has grown into one of the largest departments in the university. The Department of Biology's research focus is in the areas of Biological Control, Immunology, Medical Mycology, Molecular Genetics and Plant Biotechnology (National University of Maynooth, 2007b).

The Department of Biology offers prospective students several four year B.Sc. degree courses; a BSc (Single Honours)/ BSc (Double Honours) (in which students are educated in a wide educational range in modern biological activities, including Evolutionary Biology, Microbiology, Plant Biology, Bioethics and Biotechnology), a Denominated Honours Degree in Biotechnology, and Denominated Honours Degree in Genetics & Bioinformatics. The postgraduate degree options available through the department include a taught MSc in Immunology & Global Health, and research MSc and PhD degrees (National University of Maynooth, 2007c).

C.6 TRINITY COLLEGE DUBLIN
Trinity College Dublin (TCD) is Ireland's oldest university, being established in 1592. There are five academic faculties in TCD, two of which are related to biotechnology (Trinity College Dublin, 2007a).

C.6.1 The Faculty of Health Science

The Faculty of Health Sciences brings together four schools, the schools of Medicine, Dental Science, Pharmacy and Pharmaceutical Sciences, and Nursing and Midwifery. The faculty has close alliances with two Dublin teaching hospitals; St James's Hospital and the Adelaide and Meath Hospital, Dublin incorporating the National Children's Hospital (AMNCH) at Tallaght (Trinity College Dublin, 2007b).

C.6.1.1 The School of Pharmacy and Pharmaceutical Sciences

Established in 1977, the School of Pharmacy and Pharmaceutical Sciences offers prospective students a B.Sc. in Pharmacy, and several postgraduate degree types: M.Sc. and Diplomas in Pharmaceutical Manufacturing Technology and Pharmaceutical Analysis, and a M.Sc. in Pharmaceutical Technology (Trinity College Dublin, 2007c, 2007d).

C.6.2 The Faculty of Science

The Faculty of Science facilities include the East End Building, located on the main TCD campus. This building houses the School of Pharmacy, the Smurfit Institute of Genetics, and the Biology Teaching centre (Trinity College Dublin, 2007e).

C.6.2.1 The School of Biochemistry and Immunology

The School of Biochemistry and Immunology was established in 2005 through the joining of the existing disciplines of Biochemistry and Immunology. The school's research programmes include Folic Acid Biochemistry, Structural Biology, Neurochemistry, Biotechnology and Vaccines. The school offer three undergraduate degree programmes to prospective students in Biochemistry with Structural Biology, Biochemistry with Cell Biology and Biochemistry with Immunology. The School also offers a research M.Sc. (Trinity College Dublin, 2007f, 2007g, 2007h, 2007i).

C.6.3 The Vice-Deanery of Genetics & Microbiology

This Vice-Deanery of Genetics & Microbiology comprises the Smurfit Institute of Genetics, and the Department of Microbiology (Trinity College Dublin, 2007j).

C.6.3.1 The Smurfit Institute of Genetics

Established in 1998, the research and teaching programmes of the Institute of Genetics encompasses molecular, cellular, developmental, behavioural, medical, psychiatric, population and quantitative genetics. The institute offers two B.A. undergraduate degree programmes in Genetics and Human Genetics (Trinity College Dublin, 2007k, 2007l).

C.6.3.2 The Department of Microbiology

The Department's research topics include molecular biology of pathogenic microbes, preventive medicine, and microbial systems biology. The Department has established extensive research alliances with the Unit of Clinical Microbiology at St. James's Hospital. The Department's undergraduate programme is a 4 year B.A. in Microbiology. The Department's postgraduate programmes include research M.Sc. and Ph.D. programmes (Trinity College Dublin, 2007m).

C.7 UNIVERSITY OF LIMERICK

The University of Limerick (UL) was established in 1972, it became a university in 1989 (University of Limerick, 2006).

C.7.1 The College of Science

The College of Science includes extensive teaching and research programmes in a wide range of scientific areas including Biochemistry, Environmental Sciences, Pharmaceutical and Industrial Chemistry, and Food Science & Health. The College's research focus includes the environment and biosciences (University of Limerick, 2007a).

C.7.1.1 The Department of Chemical & Environmental Sciences
The Department's research activities include electrochemistry, organic chemistry and industrial biochemistry. The Department offers undergraduate B.Sc. degree courses in Pharmaceutical and Industrial Chemistry, Industrial Biochemistry, and Environmental Science (University of Limerick, 2003: 2007b).

C.7.1.2 The Department of Life Sciences
The Department BSc degree courses in Food Technology, and Equine Science (University of Limerick, 2007c, 2007d).

C.8 THE ROYAL COLLEGE OF SURGEONS, IRELAND

The Royal College of Surgeons (RCSI) was established in 1784. Since 1977 it has recognised as one of the National University of Ireland colleges (Royal College of Surgeons, Ireland, 2007a, 2007b).

C.8.1 The School of Medicine and Health Sciences

C.8.1.1 The Department of Clinical Microbiology
The Department of Clinical Microbiology was established in 1965, it is located in the RCSI Education and Research Centre and the Smurfit Building on the Beaumont Hospital campus. The department's research programmes includes basic and clinical research, with particular focus on the genetics of bacterial virulence factors and the surveillance and treatment of antibiotic resistant pathogens. The department conducts undergraduate and postgraduate teaching of medical, pharmacy and nursing students (Royal College of Surgeons, Ireland, 2003).

C.8.1.2 The Department of Molecular and Cellular Therapeutics
The Department was established in 2006 through the amalgamation of the Departments of Biochemistry and Clinical Pharmacology. The Department is engaged in wide reaching teaching and research programmes that cover the preclinical and clinical domains of the college. The Department is located on the main RCSI campus and additional facilities at Beaumont Hospital. The Department's research activities include molecular and population genetic aspects of inherited disease, metabolic diseases, cardiovascular medicine and neuroscience (Royal College of Surgeons, 2007c).

C.8.2 The School of Pharmacy

The School is engaged in biopharmaceutical science research, and offers a four year B.Sc. in Pharmacy as well as a M.Sc. in Industrial Pharmaceutical Sciences (Royal College of Surgeons, 2007d).