Towards Regional Science Policy?

The Rationale from Biosciences

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February, 2002

Prepared for Conference on *'Rethinking Science Policy: Analytical Frameworks for Evidence-Based Policy'*, **SPRU, University of Sussex, March 21-23, 2002**

1. Introduction

In this paper, the aim is to explore the likely effects upon science policy of changes in R&D caused by the rise of 'knowledge economies' (Dunning 2000; Cooke 2002). To advertise the argument beforehand, it is that the decline in R&D power of large corporations is accompanied by the rise of specialist research firms. The latter include, for example those referred to as 'discovery companies' in biotechnology, along with university and other research labs in proximity to which knowledge-intensive firms increasingly cluster. This is particularly pronounced in biotechnology, but also occurs in other knowledge-intensive sectors like information and communication technologies (ICT), new media and advanced business services. Broadcasters and *Bourses* are stronger cluster magnets than universities in the last two cases.

Continuing the argument, it will be shown that over the 1990s many sub-national (or what we will call 'regional') governance agencies developed interest and capability in formulating policies to network *Regional Innovation Systems.* To some extent multi-level governance hierarchies have evolved, as suggested in Lundvall & Borrás (1997) and Cooke et al. (2000) where national governments are mainly responsible for delivering science policy and basic research funding, while regional governance systems (involving public and private actors) deliver innovation programmes. These are usually near-market incentives to firms to build innovation networks, access co-funding and engage in joint marketing to enhance innovative potential and competitiveness. In Europe, the above authors suggested that the European Union was less directly involved than member states in basic research funding, more in Research & *Technology* Development (RTD) and, while co-funding *innovation* initiatives, leaving these to regions to deliver along with their own and any national programmes on the ground.

This 'discovery of the regional' by policy makers worldwide has been the most striking change in policy theory in the past decade (Teubal, 2001; Lagendijk, 2001; Castells, 2001). Policy probably led theory in this process as multilateral organisations like the EU, World Bank, UNIDO and OECD have promoted 'mobilisation of indigenous potential' and 'decentralised industry policy' since the late 1980s (see Begg & Mayes, 2000). Confirmation of the importance of regional agglomeration empirically and normatively by the likes of

Porter (1998) and Krugman (1995) vindicating earlier heterodoxy by Piore & Sabel (1984), and the spectacular cyclical growth arcs displayed by Silicon Valley and the various 'Silicon Valleys Offshore', convinced governments to have strategies to create more of these dynamic, innovative knowledge clusters (MEA, 1990; MIE, 1995; NESC, 1996; DTI, 1998; and various others listed in Porter, 1998). This brings hitherto disparate players like vice-chancellors, venture capitalists, academic entrepreneurs, development agencies and industry around the table to design centres of excellence and incubators, co-host innovation networks, organize 'First Tuesday' events, and take innovative start-up businesses to market through initial public offerings (IPOs).

All this means that the knowledge value chain is being *regionalised* and globalised simultaneously as happened earlier in industries like apparel, horticulture, computers and automotive products (Gereffi, 1999, 2000; Mathews et al. 2000; Humphrey & Schmitz, 2000). Whether this heralds or is tangential to the arrival of true R&D industry, as Stankiewicz (2001) has suggested is unclear but promising. In what follows, the first section will show how and why knowledge economies create regionalised innovation networks and clusters, particularly, but not exclusively in biosciences and biotechnology. In section two, the implications of this are explored for the large-scale national innovation system model of 'big science' and, for example, 'big pharma' following an expensive 'chance discovery' methodology, also involving big departmental research laboratories in universities. Then, finally, evidence is mobilised that tests whether the regionalising logic in new knowledge production has yet moved towards regional science policy and, crucially, regional science policy *funding* mechanisms. This section will show that both regional science policy and funding exist, albeit in piecemeal fashion. A model that responds to this demand within the national basic science funding remit is then identified.

2. Knowledge Economies and Their Regionalisation

A common misconception among non-regional scientists is that when regional analysis is done it inevitably means somehow ignoring other spatial, economic or political scales. As will be shown, the contrary is the actual position, particularly where science, technology and innovation are in focus. What has been shown elsewhere (Lagendijk, 2001; Cooke 2001b) is that by excluding the regional level from analysis, major innovation interactions between key knowledge generation and exploitation actors are likely to be overlooked. As Dicken (2001)

sees it, from the TNC perspective, regionalisation enables faster delivery, more customisation and smaller inventories than globalisation. But this does not mean TNCs become less global, rather they use whatever advantages may be available to them in seeking value chain efficiencies. So it is with regard to what might be termed the 'knowledge value chain' (see section three below) that this exploration is directed. What is this and how might it be changing? We know of the changed emphases in knowledge production proposed by Gibbons et al. (1994). Key differences involved are the move from Mode 1 to Mode 2 conventions like disciplinary purity to *transdisciplinarity*, organisational hierarchy to *flexibility and diversity*, and value freedom to *reflexivity*. Related to reflexivity, the authors argue, are *quality*-related questions of a new kind concerning the competitiveness of knowledge outcomes in the market, or cost effectiveness and social acceptability.

It is not easy to be definitive regarding the actuality of moves towards or into Mode 2-type knowledge production in general. Even in biopharmaceuricals, arguably the most science-based industry of all, the picture is occluded. What is clear is that there is more multidisciplinary teamwork or network formation than there was, as Powell et al (1996) and Orsenigo et al (2001) among many others show. Indeed the former go as far as to assert that 'knowledge is in the networks', a revision of the traditional primacy of codified over tacit knowledge. Orsenigo and colleagues explain this in terms of the heterogeneous nature of the cognitive skills demanded in bioscientific research. These necessarily give rise to collaborative learning through transdisciplinary network relationships. But networks are by no means non-hierarchical and their research shows how each of three types of biopaharmaceutical research network embodies hierarchy, albeit weakening but not disappearing around 1992 as new entrants began to collaborate with each other as well as with large drug development firms ('big pharma'). It is also difficult to see the fulfilment of *reflexivity* in knowledge production in biosciences, although ethical regulatory powers and company protocols to constrain 'value free' excesses in the field have clearly grown everywhere. Contrariwise, the inclination for stock market imperatives to interfere with peer review norms of scientific reporting is increasingly a pronounced mode of choice in announcement of scientific discovery.

Thus in 2001 Millennium Pharmaceuticals and Human Genome Sciences both made press announcements when experiments reached Phase 1 of clinical trials, at least three years away

from possible approval. In the past such announcements would be made on applying for approval. Also Dedicated Biotechnology Firms (DBFs) have recently made announcements on experiments still at basic research stage, such as Advanced Cell Technology's claim to have cloned a human embryo and PPL's to have cloned pigs, both in advance of peer review and publication of results. This is doubly problematic when, at approval stage, large numbers of candidate treatments are rejected, as thirty were by the US Food & Drug Administration during 2001. These included Chiron's anti-sepsis drug, Immunex's cardiac infarction treatment and Maxim's melanoma product. A US head of bioethics was quoted that 'these companies must raise enormous amounts of money and the only way to do that is to put a hard spin on any good news' (Griffith, 2002).

In the dynamic research field of biotechnology, the mode of knowledge production has shifted, noticeably from 1992 as revealed in databases such as that of Pammolli et al (2000) at the University of Siena. For example of the fifty dedicated biotechnology firms (DBFs) in the database pursuing 'designer molecule' rather 'discovery' methodologies 74% operated in global, hierarchical networks with big pharma developers. From 1992 onwards the incidence of R&D projects involving combinatorial chemistry, target based screening, genomics and genomic libraries doubled. All but one of the 26% of specialists followed the leaders after 1992, mostly in bioinformatics. Strikingly, 54% of the DBFs responsible for originating all these R&D projects were in four key US clusters: Cambridge, MA. (18%), San Francisco-San Jose, CA. (16%), San Diego, CA. (12%), and Maryland (8%). Hence we see a highly globalised, hierarchical knowledge generation model in which leading edge research is initiated by multidisciplinary DBFs in clusters linking with (often many) large pharmaceutical firms, research institutes and other DBFs as developers. It is plain that the clusters are increasingly the locus of knowledge generation.

This is underlined by stock market anxieties about the weakness of big pharma's pipeline of future products, calling into question its drug discovery model. Thus Bayer is seeking to divest its chemicals and some health care business after a poor performance in which its pharmaceuticals division suffered major income contraction when its cholesterol treatment was associated with more than one hundred deaths, inducing numerous lawsuits. Merck in 2002 planned like Bayer to focus on core competences by disposing of its retail pharmacy. And Glaxo SmithKline was simultaneously announcing that it would consider selling six of its research centres if their rate of new drug discovery did not improve. Glaxo's head of R&D

was quoted that: ‘ I am not certain that we are better than a biotech company, a small pharmaceuticals company or a university research department’ (**??????)**. The company has promised stock options to its drug discovery scientists in an attempt to mimic the entrepreneurial reward system common among DBFs. Another perceived solution to the trickle of innovation in the product pipeline is increased partnership with more flexible DBF research originators of the kind already described.

Having made the point about the apparently lumbering performance of big pharma in terms of new knowledge generation, it is also worth noting that rumours of its demise as a source of internally originated drug candidates should not be overstated. Thus despite most of the major US companies anticipating worsening performance, Swiss company Novartis announced in early 2002 that Glivec, its already successful chronic myeloid leukaemia (CML) drug also works for certain tumours. FDA hastened approval for Glivec to save the lives of leukaemia sufferers and the product was granted orphan drug status in the US and the UK for gastrointestinal stromal tumours (GIST). Novartis’ methodology for developing Glivec was a prototype for the rational drug design or ‘silver bullet’ rather than ‘chance’ mode of drug discovery. This entailed genomic research to target the precise molecule giving rise to the mutation causing CML. It seems, therefore, that Novartis as a big pharma company has some capability to mimic the kind of flexible networking in-house that DBFs have perfected in drug origination R&D projects. It is incidentally notable that Novartis operates an in-house incubator for innovative research firms, another indicator of its newer methodological approach.

However, Glivec is rather unusual in that at no stage was a DBF involved in the progress towards production of the therapeutic treatment. Rather, as may be seen in Table 1 the elapsed time from initial discovery to final approval was forty years. This is remarkably long in terms of DBF and venture capitalist expectations of the normal timescale for an average biotechnologically derived drug, at some ten years or so from proof of concept to hoped-for IPO. The techniques described above, particularly combinatorial chemistry that allows vast numbers of compounds to be rapidly and systematically screened through high throughput screening (HTS), applied also to methods for sequencing genes, allow for the probability of a considerable speed-up in the process. It is thought that DBFs have advantages in swiftly bringing together networks of distinctively skilled researchers and technologists to target specific molecules. The manner in which Genzyme in Cambridge, Massachusetts did this for

Gaucher's disease by tracking down appropriate genetic material in the ovaries of Chinese hamsters is a case in point has been documented elsewhere (Cooke, 2001c). The returns from success at an annual rate of over $500,000 per treatment are enormous and, as Porter (1998) argues there is less difficulty ending projects in DBFs when their 'burn rate' leads to them running out of resources than in large corporates where project-inertia makes unsuccessful ones much harder to terminate. Thus the attractions are clear to big pharma of putting-out research by funding many small DBFs, just as they are to latter who depend on it as a systemic mode of financing their R&D.

However, as Table 1 shows it was university and private research institute scientists that conducted the knowledge generation work that resulted in Novartis releasing the world's first approved drug directly to turn off the signal of a protein known to cause cancer. In other

Date	Institution	Name	Indication
1960	U. of Pennsylvania	Nowell / Hungerford	Blood Chromosome 22 'Philadelphia Chromosome'
1973	U. of Chicago	Rowley	C22 translocated to C9 discovery
1986-7	Whitehead Institute Cambridge MA	Baltimore	Bcr-Abl Protein: Tyrosine Kinase (Cell Regulator)
1992	Dana-Farber Cancer Institute, Boston	Druker	Bcr-Abl > CM leukaemia; mutant enzyme jams cell-signals discovery.
1993	Oregon Health Sciences University	Druker/ Ciba-Geigy	Reagent & inhibitor for Tyrosine Kinase activities
1993	Ciba-Geigy	Leyden/Matter	ST1571 inhibitor compound (Glivec) selected
1998-2000	Novartis	Druker	Clinical Trials & FDA approval
1998		Nowell/Rowley	Lasker Medical Research Award

Table 1: Institutional and Corporate History of Novartis CLM Treatment 'Glivec'
Source: Journal of the National Cancer Institute, January 5, 2000
http://www.nci.nih.gov/clinical_trials

words, the ‘rational drug design’ approach pioneered in cancer treatment by Novartis was really the culmination of university and research institute processes of origination, and final development through the company. Though it started as ‘chance' discovery of the Philadelphia chromosome, it evolved into a process in which precise molecular targeting became possible. This is expected to become an important, possibly the paradigmatic methodology in the post-genomic era.

In the Glivec case the importance of particular centres of research excellence in a strong biotechnology region like Greater Boston is evident. Key milestones were reached in the 1980s and early 1990s, first at the Whitehead Institute (Cambridge), subsequently co-leader of the Human Genome project, and the Dana-Farber Cancer Institute (Harvard), in identifying and then understanding the mechanism causing a mutant enzyme to jam the signal hat normally prevents massive over-production of white blood cells, hence CML. This built on the prize-winning research elsewhere that first identified and second, found where the key piece of missing DNA had translocated, which was a valuable research by-product. Thereafter, the main development technology moved with Brian Druker, the holder of the reagent that matched Ciba-Geigy’s inhibitor compounds for Tyrosine Kinase activities, from Harvard to Oregon and Basel, Switzerland. Comparable research clustering occurred in San Diego around the Scripps, Salk and Burnham Institutes, San Francisco in relation to the University of California Medical School and continues in, for example, Seattle in relation to the Fred Hutchinson Cancer Institute and Cambridge, UK in relation to many but particularly the MRC Molecular Biology Research laboratory which has hosted eleven Nobel prize winners in its time.

3.Strategic Science Policy and Science Funding: Do Regions Matter?

It has been argued thus far that knowledge production is becoming rather strongly regionalised in particular clusters. This is because of the growing importance of university and research institute laboratories to clusters of DBFs that exploit and commercialise basic scientific knowledge, with the support of venture capitalists and other business or legal services. Simultaneously, possibly more distant multinational pharmaceuticals companies are investors in milestone payments that fund the research in exchange for future expectations of licenses or acquisitions. Thus the innovation system in this sector is both highly regionalised, for research and early exploitation, and highly globalised for development and, later,

distribution and marketing. So much is this the case that stock markets are downgrading stock in large pharmaceuticals firms, and DBFs are increasingly seen stoking up their share values or prospects by what some see as premature announcements of possible breakthrough experimental results or discoveries.

This analysis exposes national innovation systems to question in ways foreshadowed by Nelson (1993, 3) when asking if the concept '…. made any sense nowadays? …. the presumption and the reality may not be aligned'. Commenting on this, Rip (2002) refers to it being a *leaky* system in which the innovation dynamics, as we have seen, are neither contained by nor expressed only at national level. Far from it, '…. a national innovation system … is a mosaic of sectoral systems and networks, with a national boundary imposed upon them' (Rip, 2002,124). Nevertheless, sovereign national governments allocate substantial amounts of research funding to science because of national political priorities, international scientific trends (and competition), and because they get a good rate of return of up to 40% in some estimates, for civilian application (David, Mowery & Steinmuller, 1992; Mansfield, 1991). We know from numerous past studies of flows that most of this funding tends traditionally to end up in metropolitan areas (Hall et al., 1987; Hilpert, 1991; Malecki, 1991; Kleinknecht, 1996) like London's 'Golden Triangle' with Oxford and Cambridge, where over half went in the 1990s, or South Paris with an even greater functional dominance in most scientific research, especially biotechnology (Lemarié et al., 2001).

Similar flows to (European) 'Islands of Innovation' were detected in the 'Archipelago Europe' programme (Costello, 1991), and subsequent European Union S&T funding data analysis showed those regions in receipt of the largest share of Framework 4 budgets becoming more regionally concentrated in metropolitan centres than those for Framework 3 (European Commission, 1997; 2001) when the 'Archipelago Europe' programme was extant. However, the question being raised in this paper concerns not these well-known top-down science budget allocations as national and supranational science policy priorities were implemented in the past. Rather it is whether there is evidence of a growth in *regional* science policy and consequent allocations. Moreover, if there is, does it take a *form* substantially different from the largely state or pooled public (EU) one described above? Thus if globally networked regional clusters predominate in biotechnology, as there is abundant evidence they do (see Swann et al., 1998 and papers in *Small Business Economics,* Special Issue, 2001) is this leading to new policy thinking? Is 'ground-up' strategic science

policy and funding within specialist 'knowledge economy' regions occurring for other sectors (Cooke, 2002)? In the space available this can only be explored for biopharmaceuticals, but the resulting evidence makes the hypothesis worthwhile exploring further.

Strategic research (as defined by Irvine & Martin, 1984) has become less military and more civilian since the end of the Cold War. It is arguable it has had to become more 'relevant' in the sense of more market-facing and ethically-sensitive, as we have seen (Gibbons et al., 1994). Importantly, it has allowed a repositioning of major science policy priorities towards the health rather than the defence of civilian populations. Mowery & Ziedonis (2000) show how the surge of US federal research funding in biomedical science significantly outweighed the effect of the Bayh-Dole Act on intellectual property in raising patenting and licensing even before the 1990s. Bayh-Dole seems mainly to have increased the number of useless patents, judging by their citation analysis. Cockburn & Henderson (2000) quote Irvine et al.'s (1990) statistics showing that by that time the US spent nearly 50% of its national academic and related research budget on Life Sciences. By 1999 it was twice the 1987 magnitude at $14.8 billion (DTI, 1999 quotes the NIH budget for 1999 as $15.6 billion, a $2 billion or 14.4% increase over 1998). By 2001 it was over $20 billion, causing the following comment from the director of science policy at the American Association for the Advancement of Science:

> 'As a result, NIH is now the 800-pound gorilla of the research community, accounting for 42 percent of all non-defense R&D, more than half of all federally-funded basic research, and nearly two-thirds of all federal support for R&D in colleges and universities' (Teich, 1999).

The Bush administration's budget request for the NIH in 2003 was $27.3 billion (51% of federal basic research), a $3.7 billion increase over 2002 (Burnell, 2002). To this must be added portions of NSF, NASA and Department of Energy (human genome) research budgets. It is abundantly clear that health care is driving the US basic research-funding portfolio as never before. In the UK and Germany totals for biosciences research are of the order of $1 billion annually.

The very large sums of research funding now going to regional biosciences/biotechnology clusters in the US and their younger equivalents in European countries give these locations both the resources and expertise to develop as implicit if not explicit 'Centres of Excellence'.

Because of the perceived relevance and political virtue of life sciences research health research budgets have mushroomed. Correspondingly, financial pressure on hospitals to treat not conduct research on patients (see below) has undermined clinical scientific opportunity to take advantage of the molecular biology revolution. Moreover the growing evidence that university or public laboratory research with associated spin-off DBFs is at the heart of knowledge generation and exploitation, leaving big pharma with drying pipelines and a main role as developer/marketer in the 'knowledge value chain' has a determinate effect. Hence, such Centres of Excellence attract further funding, from their regional governments, from bilateral industry research investments (e.g. Novartis and UC Berkeley, $25 million), from endowed institutes and medical foundations, which in the shape of those such as the Howard Hughes Medical Institute ($13 billion endowment) and the Wellcome Trust (£600 million annual expenditure) are of major significance. The latter explicitly operates a Centres of Excellence programme, which in the UK involves the universities of Glasgow (parasitology), and Edinburgh (cell biology) in Scotland, Manchester (cell matrix), Cambridge (cancer jointly with Cancer Research Campaign), Oxford (human genetics) and London (history of medicine). Wellcome further funds eight 'Regional Science Centres' (educational science marketing centres) in Dundee, Glasgow, Newcastle, Manchester, Birmingham, Bristol and London. The Howard Hughes Medical Institute primarily funds researchers rather than

Foundations	Grants 1999	Endowment 2000	Corporate Foundations	Grants 2000
1. R.W. Johnson	$372 m	$8.8 bn	Aventis Foundation	$41.6 m
2. D&L Packard	$114 m	$9.8 bn	Proctor & Gamble Fndn.	$30.4 m
3. California Endow.	$91 m	$3.5 bn	Merck Fndn.	$28.8 m
4. Whitaker Fndn.	$50 m	NA	Pfizer Fndn.	$25.5 m
5. B&M Gates Fndn.	$48 m	$21.2 bn	Eli Lilly Fndn.	$17.1 m
6. Burroughs Wellcm.	$37 m	$0.8 bn	Bristol-Myers Squibb	$15.8 m
7. Rockefeller	$36 m	$3.6 bn	Monsanto Fndn	$14.0 m
8. D. Reynolds	$35 m	$1.3 bn	Medtronic Fndn.	$12.0 m
9. Starr	$34 m	$4.5 bn	Abbott Fndn.	$10 .0 m
10. WM Keck	$32 m	$1.5 bn	Glaxo Wellcome	$7 .0 m

Table 2: Top Ten US Medical Research Foundations and Corporate Foundations
Source: S.Lawrence (2001) *Health Funding Update*, New York, The Foundation Centre

Centres but has laboratories at the universities of Maryland, California-Los Angeles, Washington-St. Louis, Rockefeller and internationally.

In the US there are, of course, numerous other charitable and corporate medical foundations, the largest of which are shown in Table 2. Grants from these augment the large scale NIH awards and add further to the resource base of Centres of Excellence. Indeed the more a regional centre is designated as such the more likely it is to attract further funding. The UK is unique in having a single charitable health research trust that spends per year an equivalent amount to sums the top ten US charitable foundations spend together. This makes the Wellcome Trust a strategic science funder and policy maker in its own right in the UK. It could be argued to be as important as the UK government in determining bioscientific and health research expenditure flows, as a glance at selected highlights of its funding portfolio during 2000-2001 demonstrate (Table 3).

Date	Headline	Funding	Recipients
April 2000	Joint Infrastructure	£129 million	Ulster, Dundee Birmingham JIF
July 2000	Joint Infastructure	£225 million	New (SRIF) Prog.
July 2000	Genome Bioinformatics	£8 million	Cambridge (Sanger)
October 2000	Genome Sequencing JV	£8 million	Cambridge (Sanger)
October 2000	C. for Molec. Medicine	£7 m annually	Cambridge (Addenb.)
April 2001	Science Centres/ Infrastr.	£76 million	Scottish Universities
May 2001	Scientific Rsch. Facilities	£125 million	34 SRIF Grants
July 2001	Synchrotron	£110 million	Oxford
October 2001	Post-Genomic Research	£300 million	Cambridge (Sanger)
November 2001	Clinical Research Facility	£ 3.8 million	Southampton

Table 3: Wellcome Trust Grant Announcements 2000-2001
Source: Wellcome Trust

The key point to note from Table 3 and below is the trend towards regional Centres of Excellence and the manner in which in the UK the Wellcome Trust increasingly sees its role as regenerating parts of the national innovation system for health which has been damaged by a lack of policy or underfunding crises that have had negative effects on important parts of the national system, especially the National Health Service. Thus although, as Table 3 shows for the May 2001 entry, Wellcome grants under the SRIF scheme were diffused, a third of the £125 million, some £40 million was awarded to Leicester, Edinburgh, Leeds and Manchester (UMIST) universities, seven awards went to London, three to Oxford, two each to Sheffield, Cambridge and Cardiff, and a further two to Edinburgh. This reflects an emergent picture underlined in the UK government report on biotechnology clusters (DTI, 1999). That proposed regional centres in the above-named places plus regions with collaborating regional universities as in Yorkshire ('White Rose' partnership) with Sheffield (2 awards), York (1 award) and Leeds (1 award) or in Scotland Glasgow (1), Dundee (1) along with Edinburgh, and, in Wales, one centre based in Cardiff, could expect to be candidates for development outside the 'golden triangle' of Cambridge-Oxford-London.

This is predominantly where, given appropriate quality bids, Centres of Expertise may be expected to become Centres of Excellence, and the move, first successfully demonstrated with the establishment of numerous Centres of Research in Stanford University (Gibbons, 2000) of specialist research away from large university teaching departments gets under way. This also applies to another big casualty of the changing research mode, clinical research in hospitals. In the UK, the latter is underlined in Wellcome's policy of funding Clinical Research Facilities (CRFs) because:

> '…. while the UK has the inestimable advantage of a National Health Service… the financial pressures on the NHS and healthcare reforms have created many obstacles to patient-oriented research. Not least of these is the enormous pressure on beds; patients requiring treatment obviously take priority, leaving no spare capacity that could be used by researchers.'(Wellcome Trust, 2002)

The Southampton facility (Table 3, November 2001 entry) is one of five CRFs, the first opened earlier that year in Edinburgh; the others will be at Manchester, Birmingham and Cambridge. Thus regionalisation of special clinical research as well medical and bioscientific Centres of Excellence is occurring as a policy initiative being implemented by the Wellcome Trust in response to changes induced in the traditional model by government health policy. Specifically it is seeking to maximise patient treatment capability on internationally low

public expenditure, at the expense of clinical research. Thus the government's Culyer Task Force found ways of segmenting costs of NHS research and paying for it with a levy on healthcare purchasing. These funds are only to be used for recurrent costs, while foundations and research councils cover direct research costs. Absence of funding for fixed capital developments led to Wellcome Trust policy to invest in CRFs. They are modelled on US General Clinical Research Centres (GCRCs) of which there are 78. Their existence was initiated by US health insurance companies' refusal to pay for research in hospital beds, and now even outpatient clinics to which research moved are too busy for research. GCRCs cost $170 million per year to run and are funded through grant applications from Centres to the National Institutes of Health. The Wellcome Trust programme is funded at £20.5 million.

Thus, as government funding constraints have placed the NHS under ever greater financial pressure, clinical research capability is facing diminished capacity. Providers are thus becoming more entrepreneurial in their response and seeking significant funding from non-public sources, notably foundations like the Wellcome Trust co-funded for CRCs thus far by university hospitals and local health service administrations (the NHS Trusts). Having large patient databases for research is a necessity in the new world of molecular medicine and rational drug design. Thus it is not difficult to see the evolution of regionalised 'knowledge value chains' from basic university or research institute Centres of Excellence such as the Sanger Institute is for genomic and post-genomic research, through to medical and clinical research at Centres of Excellence in university hospitals or schools of biosciences, to biotechnology institutes or Centres, and Gene Centres or Gene Parks where exploitation and commercialisation are conducted by academic entrepreneurs interacting with clusters of DBFs.

The model can be observed in Greater Boston where all these facilities are in place, where over $1 billion in research funding alone is spent annually, much of it in collaborative partnerships among universities, special research Centres of Excellence (e.g. the Whitehead or Dana-Farber Institutes at MIT and Harvard), large hospitals like Massachusetts General or Brigham and Women's, GCRGs, incubation and successful start-up and more mature biotechnology firms like Ariad, AlphaGene, Dyax, Genetics Institute, Genome Therapeutics, Genzyme and Progenitor. Among the non-regional research partners are Aventis, Bayer, Bristol-Myers Squibb, Chugai Pharma, DuPont, Merck, and Pharmacia. These are increasingly engaged as investors, developers (though see below, section five), distributors

and marketers for the products and services of the regional biopharmaceuticals innovation system in Massachusetts, focused on Greater Boston and with its epicentre at Cambridge (Cooke, 2001a). Massachusetts has for many years had a regional science policy to support with tax-breaks and other incentives high technology industry, once seen as responsible for the 'Massachusetts Miracle' in mid-sized computers, and now experiencing a resurgence through the promotion of biotechnology, biomedical and venture capital 'clusters' (Best, 2000; Porter, 1998). Harvard Business School and especially Michael Porter, has been closely involved in advising successive Governors, notably Governor Weld, in developing strategic science policy and supporting or supplying knowledge whether in the form of consultancy reports, global competitiveness indices and technology and innovation benchmarks to offer regional foresight and track global progress (see, for example, Massachusetts Technology Collaborative, 1999 whose knowledge economy indicator reports were adopted in the UK by DTI and by OECD as forerunners of their knowledge economy indicator metrics).

4. Regional Science Policy: The Basic Model and Some National Variants

It has been argued thus far that bioscience underwent a cognitive, methodological and technological evolution that appears to have been expressed as an empirical punctuation point around 1992, though much of that change had been in the pipeline well before that. Some move into Mode 2 knowledge production became evident as transdisciplinary research networks among research Centres of Excellence, academic entrepreneurs and successful start-up DBFs began accessing dynamic externalities in the form of knowledge spillovers from co-location in geographical proximity to exploit opportunities for rational drug design. However, such networks remained hierarchical both because of élite science (the 'star' system; Zucker et al. 1998) and the continuing involvement of big pharma companies, less as originators that as developers of therapeutic solutions coming from biotechnology. The argument then evolved to discussion of a 'knowledge value chain' in life sciences spanning the arc from basic post-genomic and proteomic research through clinical research and treatment to innovation and commercial exploitation by clustered DBFs. It was then argued that this exists in a few regions of the world, that Centres of Excellence are competitive and attract or possess large financial resources, and that their regional and technological innovation system governances have explicit or implicit science policies. Other governances will seek to emulate these leaders and have, indeed begun doing so.

In the US and Europe the regional 'Clusters of Excellence' include Southern California, centred on San Diego, in Northern California it is Silicon Valley, and in Massachusetts, Boston. In Europe such clusters are found, on a smaller scale than the US, in the UK at Cambridge in the Eastern England regional development agency (RDA) area, possibly also Oxford (South East RDA) and Scotland (a triangle including Dundee, Edinburgh and Glasgow), in Sweden Stockholm-Uppsala and in Germany, Munich in Bavaria although two other *BioRegios* also exist (Dohse, 2001; Cooke, 2001a; 2002). In these innovative 'biotech cities', it is vital to recognise the regional innovation systems in which they operate. These supply finance (e.g. Bavaria sold its state energy company and established a high-tech fund, which invests in biotechnology [and ICT] research and commercialisation activity), in Scotland, as we shall see, 'regional' funds for implementing its science policy for biotechnology are pooled among its RDA, Parliament and university funding body (SHEFC). As part of its modest move to regionalise administratively, the Swedish national government in 2001 established VINNOVA, the Swedish Development Agency for Innovation Systems with responsibilities to invest in *regional*, technological systems in biotechnology and other advanced technology sectors. There is also a unique cross-border policy and R&D body (Øforsk) to exploit the new bridge, by building an Öresund regional biosciences innovation system between Denmark's 'Medicon Valley' near Copenhagen and the Ideon Science Park bioscience cluster at Lund near Malmö, where AstraZeneca has a large R&D facility. We shall explore a further Nordic case in depth below, which is the case of Finland.

Observing these developments, regions with aspirations and some perceived or actual potential to emulate the élite can relatively easily be identified. Two in the US are worth briefly exploring. These are North Carolina and Maryland, both of which have emergent regional biotechnology innovation systems. In the case of North Carolina, there has been an effective science policy since the 1950s when the Governor got approval for the Research Triangle Park (RTP). This had the limited objectives of attracting R&D jobs with no presumption that synergies would flow among the facilities locating there. Subsequently major support was given to boosting the research capabilities of the three universities, Duke, UN Chapel Hill and NC State, but especially the last two public ones. Duke's private endowment has ensured that its medical school and bioscientific research profile have prospered, while in the 1990s NC State was the recipient of major state funding to develop it as a Technology Campus with industrial R&D laboratories co-located with science and

technology departments. In between, in 1981, the North Carolina Biotechnology Centre (NTBC) was established on RTP (as, at approximately the same time, were the NC Supercomputer and Electronics Centres). NTBC was not a research but a commercialisation facility. In early 2002 NTBC housed some thirty biotechnology businesses, including sites of Aventis, BASF, Bayer, Biogen, Eli Lilly and Glaxo SmithKline among the 90 in theRTP and broader Raleigh-Durham-Chapel Hill area, and 142 in the State.

Duke University Medical Centre is prestigious in basic and clinical biomedical research with cancer and urology being leading fields for which the Centre is ranked sixth in the US. Basic scientific research is wide ranging and operates in 38 laboratories including biochemistry, cell biology, genetics, immunology, microbiology neurobiology, pharmacology and cancer biology. The Duke Comprehensive Cancer Centre is accredited by the National Cancer Institute (NCI) and conducts clinical research, patient care and teaching in cancer immunobiology, prevention, detection and control, cell regulation and transmembrane signalling, cellular and structural biology, experimental therapeutics, molecular oncology, and cancer genetics. UNC School of Medicine is unofficially ranked 22nd in the US and its strongest research field is biomedical engineering in which expertise is found in medical imaging, biomedical computer communication, medical informatics, neuroscience engineering, bioelectronics and sensors, physiological system modelling, biomaterials and real-time computer systems. The Lineberger Comprehensive Cancer Centre is one of the NCI national network of Cancer Centre Programme facilities specialising in biomedicine.

Maryland is also an important US centre for bioscience, hosting 210 bioscience businesses, half in research services, testing and contract manufacturing, two strong university systems, organisations like FDA and NSF, and a large number of federal research laboratories, notably the NIH system. Much of this activity is clustered along the I-270 ‘Technology Corridor’ (Bethesda-Rockville-Frederick) and around Johns Hopkins University in Baltimore. The Howard Hughes Medical Institute research laboratories are nearby in Chevy Chase. NIH has 25 institutes and centres, including the US National Human Genome Research Institute at Bethesda and the National Cancer Institute at Rockville. The Johns Hopkins University is ranked first among US universities in receipt of federal R&D funds, the School of Medicine is first in receipt of NIH extramural funding, and unofficially ranked second nationally after Harvard Medical School. Its research expertise is focused on AIDS, biomedical engineering, cancer, clinical immunology, genetics, molecular biology, neuroscience, organ

transplantation, and urology. The University of Maryland, Baltimore is a rapidly expanding biomedical research centre in partnership with the University of Maryland Medical School System, the Veterans Administration Medical Centre, and the Medical Biotechnology Centre, specialising in molecular genetics and human molecular biology. There is also a UM Biotechnology Institute specialising in basic science applications to health, marine environmental and agricultural biotechnology, protein engineering and structural biotechnology.

Science &Technology Policies: Market Facilitating

Both states inherited buoyant technology markets from past public investment decisions. On the basis of these strengths and to a high degree influential upon them, both states are among the thirteen in the US to have adopted statewide strategic science and technology policies, from between 1991 and 1995 (American Association for the Advancement of Science, 1999). The main goal of each policy has been enhancement of economic growth and improving standards of living by capitalising on the state's research base. Policies recognised the importance of sustaining and strengthening the R&D capacity of university research and training. In North Carolina, building on the success of Research Triangle Park, strategy focused on further stimulating exploitation of biotechnology and other technologies, and continuing to strengthen R&D capacity. Strategies emphasised stimulating indigenous entrepreneurship and promoting generative rather than redistributive growth. Maryland's strategy included recommendations for exploiting commrcialisation potential of technology from its strong universities and federal research laboratories. Both Maryland's and North Carolina's policies were initiated by their Governors, but others were the result of private initiative. Usually they began by analysing the strengths and weaknesses of the state economy and research infrastructure. In many cases they then went on to identify knowledge-based industry clusters, arguing that the state's economic base was passing from an old to a new economy character. Strategic policies were proposed to meet the challenge. In North Carolina's case this involved seeking input from six task forces and nine focus groups, using the North Carolina Alliance for Competitive Technologies s the governance body for the process. Both Maryland and North Carolina included specific outcome measures, such as quantifiable growth rate of technology businesses, industry support for university R&D, and new start-up companies. However the AAAS assessment of these policies was that they were insufficiently detailed and mostly failed to address issues of social exclusion.

In 2000, North Carolina published *Vision 2030: Science and Technology Driving the New Economy* based on a new approach emphasising *visioning* based on a statewide foresight options process. It will be shown later that this is becoming a more widely adopted approach to regional science policy, having been pioneered in Massachusetts, advised by Michael Porter's *Monitor* consultancy. It also involves cluster identification and regional stakeholding to attempt to commit industry and university administrations to invest in co-funding actual initiatives intended to be implemented. UNC Chapel Hill organised regional conferences, focus groups, cluster analyses, global benchmarking, and produced the North Carolina Innovation Index. Recommendations included evolving a knowledge economy through supporting venture capital, public funding and tax incentives, marketing North Carolina globally as a knowledge economy, and designing a globally competitive R&D tax credit. Maryland's newest policy statement *The Maryland Technology and Innovation Index* was launched in late 1999 with similar style and content, using comparative benchmarking indicators addressing performance, dynamics and resources using the Maryland Technology Alliance of private sector, academic, federal and state government organisations as the catalyst.

Science Strategy: Science-Led Growth from Below

Devolution in the UK has opened up a responsibility for democratically elected Executives in Scotland, Northern Ireland and Wales to formulate science policies. Wales developed the EU's first Regional Technology Plan in 1994 and relies on an updated version under the Regional Innovation Strategy 2 programme from Brussels. The Welsh strategy has guided the establishment of expenditure patterns on technology and innovation under the Structural Funds Objective 1 action lines. This includes establishing a Knowledge Exploitation Fund, technology counsellors in universities and other infrastructures in support if *innovation* rather than basic science strategy. Northern Ireland is in a better position because of the existence of the *Industrial Research & Technology Unit*, which, through its annual corporate planning process designs technology and innovation, if not science policy in the region. It is noticeable that, despite its peripherality and political troubles, Northern Ireland has developed a discernible science and technology policy not unlike but more piecemeal than Scotland's. Thus biosciences and ICT (especially telecommunications and Internet software) have been

supported with research funding from IRTU, contest-successes for UK grants to enhance academic entrepreneurship, and the construction of nine incubators for the two target sectors. The necessity for regional science policy in both Wales and Northern Ireland is demonstrated by the evidence that at £34 and £24 per student respectively, the UK government's low investment in science funding there compares unfavourably with the £44 per head in England and £58 in Scotland. Research performance, measured since 1986 in the UK Research Assessment Exercise, explains the disparities to some extent. In this context, it is noteworthy that Northern Ireland's most significant biomedical research initiative, the University of Ulster's £14.5 million Centre for Molecular Biosciences was equally co-funded by the Northern Ireland 'Support Programme for University Research' fund and *Atlantic Philanthropies*, an Irish-American foundation which, since 1982, has invested $1.3 billion in higher education worldwide, 28% of which was in Northern Ireland and the Republic of Ireland. The donor, Charles Feeney, also funded the Sinn Fein office in Washington. The university's vice-chancellor, bemoaning a 20% decline in the region's funding for academic research through the UK system said: 'With devolution, we have found greater awareness of the importance of the research base than when we had direct rule' (Farrar, 2002).

Scotland was first in the UK to seize the opportunity to develop a regional science policy, its Minister of Science publishing in January 2001 *A Science Strategy for Scotland.* It was preceded by a report in 2000 from the Science Strategy Review Group and informed by Scotland's Science Policy Unit. The report shows that about £800 million is spent on scientific research in Scotland annually, and that Scottish universities won £141 million or 11% of the UK Research Councils budget in 2000, about twice the country's share of the UK population or GDP. The *Science Strategy* makes it clear that although Scotland's economy performs at about the UK norm, market forces alone cannot be relied on for economic growth to occur but that Scotland's basic science advantage and government activity more generally have to be directed increasingly at sustaining world scientific leadership in a few feasible areas and raising commercialisation and entrepreneurship opportunities arising from science. The report prioritises bioscience and genomics, medical research, and e-science as the three areas of world leadership in basic science that the Executive will support in particular. This means maximising Targeted Science Research Expenditure for these areas, including improving relationships between University and Biological Research Institute research facilities in Scotland. To assist this the Executive commits itself to investment in Scotland's joint Science Research Investment Fund.

Making an important commitment towards science funding in the UK as a whole, it aims to assist in setting in place a more transparent research funding methodology to ensure underfunding of the kind widely perceived to have bedevilled UK science for decades cannot happen again. Scotland's problems of low industrial R&D and a high proportion of small businesses are to be moderated by connecting to economic growth initiatives such as the Scottish Executive's *The Way Forward-a Framework for Economic Development; The Knowledge Economy Cross-cutting Initiative*; and the *Digital Scotland Task Force.* Accordingly, it commits to keeping the 'Proof of Concept Fund' (see below), setting up a National Health Service Technology Transfer Office, revitalising UK-originated small business research and technology awards, assisting academic entrepreneurship, using Foresight to identify future scientific challenges and opportunities, and recruiting investment and scientists from overseas.

This is clearly a more interventionist set of commitments than are discernible in the more 'market-following' policies described previously. As in Northern Ireland and Wales, government has to do more because of market arrest, in a context of greater reliance on market forces where they are strong, which in the UK means in effect, the aforementioned 'Golden Triangle'. Scotland was advantaged in bringing forward its fairly robust commitments to science support by preceding work done by Scottish Enterprise, the RDA, in commissioning a vision-led clustering strategy from *Monitor* in the early 1990s. This introduced a new approach to 'knowledge economy development' by encouraging focus, also to some extent foresight, and introducing envisioning methods to identify opportunities for global competitiveness, mobilising stakeholders in a partnership methodology, and forming consensus on actions and resources to be implemented by committed leadership in specific spheres. The £30 million 'Proof of Concept Fund' established in 1999 is a good illustration. It allows scientists in the prioritised sectors, among which biotechnology and ICT were the first to benefit, to buy-out teaching and administration time to conduct research leading to academic entrepreneurship. The fund was formed from contributions by Scottish Enterprise, The Scottish Executive and the Scottish Higher Education Funding Council. Notably, no private co-funding was committed to the fund. Scottish Enterprise estimates in 2002 show that fourteen biotechnology projects have been funded and that, since March 1999, 28 new biotechnology companies have been created, equivalent to a growth rate of 30% per annum. This compares favourably with the European average of 17% per annum over the same

period. Scotland is home to 20% of the biotech companies in the UK and is recognised as one of the fastest growing regions for start-ups. Thus far, policy to support commercialisation of bioscience has been successful; also we have seen that Scotland has received major funding, including both Research Council and Wellcome Trust grants in support of its leading university Centres of Excellence and their research. Scotland now has a Strategic Science policy and it remains to be seen if the effectiveness shown without one can be enhanced consequentially.

This can be compared briefly with the rather longer-established science and innovation policy approach practised at province level in Canada, notably Quebec, which has exercised the greater autonomy in this regard, and Ontario. In both cases, strong scientific research bases can be found at provincial level, centred on Montreal and Toronto. In the Quebec case, Latouche (1998) pointed to a rising R&D expenditure (GERD) rate having reached 1.79 compared to Ontario's 1.87 and Canada's 1.51 but much lower scientific papers production than either, presumably for reasons of limited language of publication outlets in French compared to English. Quebec's share of federal R&D extramural contracts declined 1973-1994 from 26% to 13% while Ontario's increased marginally from 50% to 51%, and Quebec's share of federal grants for science and technology were only some 36% of those in Ontario.

Neither province has a science strategy along the lines produced in Scotland, though in 1999 Ontario set up *The Ontario Science & Innovation Council* as recommended by the province's Jobs and Investment Board's report 'A Roadmap to Prosperity' report. The Council was charged with providing long-term strategic advice and leadership on policies and priorities related to science and innovation. The board consists of academics, researchers and business leaders from Ontario's knowledge economy sector. According to Wolfe & Gertler (2001) the 'Roadmap to Prosperity' report resulted, amongst other things, in a 'Superbuild Growth Fund' to inject C$20 billion to rebuild infrastructure. In 2000 C$1.4 billion were earmarked for the province's higher education sector. The fund was a partnership between the provincial administration, other public partners and the private sector. It echoed a more visionary time in the 1980s and 1990s when substantial investments were made through the Premier's Council Technology Fund in seven university-based Centres of Excellence (see also, Salter, 1998) to strengthen scientific research in provincially important sectors. However these were reviewed and by 1996 a reduced budget meant only four Centres could be sustained. Since

then, recommendations for enhanced science expenditure through the Ontario R&D Challenge Fund and the Ontario Innovation Trust has not been implemented. It may be concluded that Ontario, an early leader in implementing science policy at the regional level has thus far not evolved towards a coherent science strategy of the kind that seems now to be entering vogue.

Much the same can be said for Quebec, traditionally a somewhat corporatist governance system from which sectoral and technological analysis is regularly and consistently published by the Quebec Council of Science & Technology. However, in the 2001 *Regional Dimension of Innovation in Quebec* report it is baldly stated that:

> 'Strictly speaking the Quebec government has no overall vision, strategy or co-ordinated policy for its regional innovation capacity. Most outcomes are the result of ad hoc decision-making' (Quebec Council, 2001)

The report comments on Montreal's dominance of the province in terms of high technology employment, R&D expenditure, shares of contract research, technology transfer centres, and science indicators like patents and publications. Most support has been for innovation and generic rather than targeted, including college technology transfer centres, *Innovatech* for venture capital, tax incentives for industry innovation centres like *Optics City* and *Multimedia City,* technology observatory services and *Inno-Centre* incubators. Federal facilities and services like Regional Innovation Assistance, the fifteen Government Laboratories and Research Centre activities and the offices of Canada Economic Development are mentioned as important contributory elements of the regional innovation support system. The report recommends the production of regional innovation strategies throughout Quebec, with training support and government implementation of strategies, simplifying the innovation policy instruments and developing innovation indicators and benchmarking.

A further report from the Council on *Bioinformatics in Quebec* (2001) recommended implementing an intensive bioinformatics training programme by September 2001, introducing 10 fellowships to enable training to occur beyond Quebec, swift introduction of bioinformatics graduate study programmes, development of a network of formative research projects in genomics, proteomics and bioinformatics, tax incentives to hire bioinformatics personnel, and monitoring of Quebec's performance in each targeted sub-sector. Numerous other executive reports from the Quebec Council of Science and Technology have a

comparable flavour of being piecemeal responses to each new technology that comes along, attempting to ensure a necessary basis for engaging to some degree with the innovation dimension rather than the scientific base as such. Nevertheless it is worth keeping in mind that, as Niosi & Bas (2001) point out, that of Canada's 282 DBFs some 25% are in Toronto and 20% in Montreal, also that they have the lion's share of firms with either US or Canadian patents, and the majority of bioscience and health science academics (Toronto 1149; Montreal 780). Public laboratory patenting is strongest at Ottawa's Institute for Biological Sciences, second comes Montreal's Biotechnology Research Institute, two of the five National Research Council biosciences labs in Canada. Hence the absence of strategic regional science policy has not hindered the progress of bioscience research or exploitation as testified by the existence of well-known firms like the former Connaught Labs in Toronto and Montreal's BioChem Pharma, originator of Glaxo's leading AIDS treatment Epivir. Moreover universities with strong bioscience track records include Montreal, McGill and Laval in Quebec, and McMaster and Toronto in Ontario.

Science Strategy: Science-Led Strategy from Above

The last case to be explored is that of Finland, a small country that has emphasised the importance of developing Centres of Expertise in its regions, supporting university-centred basic research, commercial exploitation and cluster-building in biotechnology as it did with global success in relation to ICT and the rise of Nokia to global prominence in mobile telephony. The model is also one in which foresight and envisioning play a role in bringing about a consensus among business, academia and industry to invest in Centres of Expertise in locations that already show some comparative advantage. Centres of Expertise in Biotechnology arose from a Ministry of Education national research programme on biotechnology in 1987.

The aim was to develop four regional centres of biotechnological expertise by 1992, planned to be affiliated to those Finnish universities assessed to have the appropriate potential. The selected centres were at Helsinki, Turku, Kuopio and Oulu. The programme was evaluated and continued in 1996 then extended to 2000. Financing came from the Ministries of Trade & Industry, Agriculture & Forestry, and Social Affairs & Health as well as Education. Other centres were added such as Tampere and Seinajoki. The arrangement for enlargement of the network is one whereby if a municipality is sufficiently committed to serious long-term

investment in biotechnology, by funding a number of chairs in universities, for example, then provided they pass exacting tests of expertise, they can become eligible for designation and funding as a Centre of Expertise. This has led to an excess of demand for Centre designation and the programme has been terminated in consequence. Centres specialise within biotechnology such that Oulu, Turku, Tampere and Kuopio focus on medical research and co-operation with the pharmaceutical industry. Helsinki and Seinajoki specialise in agro-food biotechnology and some agro-food R&D is also performed in Kuopio, Oulu and Turku.

Tekes, the state technology agency has invested some $90 million in biotechnology, some 27% of its total investment portfolio. The Centres of Expertise programme receives $4.1 million annually from Tekes and the Academy of Finland. Thus some 40% of these two agencies' budgets is in support of biotechnology. Also, the National Programme for Research on Biotechnology, begun in 1988, invests an annual amount of some $13.5 million in biotechnology. Further expenditure on the Genome Research Programme and the Cell Biology Research programme attract $4.5 million and $1.8 million annually over six and three year programme periods respectively. In 1993, the Ministry of Education set a new Centres of Excellence standard, seeking to identify ten 'top units'. By 2000 26 had actually been established of which nine are in biosciences and biotechnology. In March 2001 a further $102 million rising to $151 million by 2006 was committed by Tekes, the Academy of Finland, Sitra (Finnish national R&D Fund), Finnish Bioindustries, and a substantial group of pharmaceuticals companies to 'Medicine 2000' addressing biomedicine, medicine development and pharmaceutical development research and technology.

Finland's commitment to evolve a strong biosciences and biotechnology capability is remarkable, with proportionately comparable shares of total national R&D budgets (some 40%) as the US. The fact that its agro-food firms are responsible for nutraceuticals innovations like anti-cholesterol product Benecol (Raisio Ltd.), lactobacter drinks and UHT infant food (Valio Ltd.), and xylite sweeteners (Danisco-Cultor Ltd.) suggests where current strength lies. Orion Pharma and Orion Diagnostica are the two leading biotechnology players, the former having the leading Parkinson's treatment *Comtess* newly-released, the latter targets the global point-of-care (POC) market for *in vitro* diagnostic products. Orion Pharma collaborates with all the Finnish Centres of Excellence, but particularly the regional centres at the Universities of Helsinki and Kuopio, the Helsinki Biotechnology Institute, and increasingly with the Universities of Tampere and Oulu – the latter also being Orion

Diagnostica's main research partner. The Finnish national innovation system is highly integrated but state-led with a knowledge value chain involving The Finnish Academy funding basic research, Sitra funding R&D, VTT conducting research and technology transfer, Tekes funding technology development, and Centres of Excellence in universities working directly with large firms, start-ups and spin-offs in clusters on state and locally funded Science and Medical Technology Parks like Hermia at Tampere, Oulu Technopolis, and Medipark or DataCity and BioCity at Turku. In the report on Finnish Life Sciences by Tulkki et al. (2001) these regional innovation systems are presented as worked models of the Finnish view of the functioning of Silicon Valley. The key difference is the involvement of large firms and public investment in the commercialisation process, substituting for an arrested market for key innovation support services. In this respect, it has been influential upon the German regional biotechnology clusters commercialisation programme *BioRegio* that similarly sought a 'corporatist' version of the 'basic research-academic entrepreneurship-venture capital' model that was pioneered in California (Dohse, 2000).

5. Conclusions

This paper started with a question about the existence and observability of a new phenomenon, regional science policy. Its likelihood was implied by a number of important changes in global politics (ending of the Cold War) scientific research funding (major transfers from defence to healthcare), knowledge production (Mode 1 to Mode 2) bioscientific research approach (molecular biology), drug research methodologies (chance discovery to rational drug design), R&D leadership ('big pharma' laboratories to university 'Centres of Excellence') and innovation leadership ('big pharma' to DBF clusters). Countless expert commentaries, most recently Dyer (2002), confirm the fact that all these changes are now established in the practicalities of life sciences and medical research and innovation, and that, for example, big pharma has not only had to come to terms with these realities, but is stumbling into even more difficulties as it tries to do so. Thus troubled US firm Bristol-Myers Squibb, in trying to do what this paper noted was industry insider expert recommendation and forge closer DBF links, invested $2billion in 20% of ImClone to access Erbitux, a colon cancer drug. But FDA approval was withheld due to faulty clinical trialing by ImClone. This has caused big pharma to question its management capabilities under arrangements where it has become mainly marketer-distributor to DBFs like ImClone, or Celltech with a similar deal with Pharmacia, and Isis Pharmaceuticals with Eli Lilly.

Attempts by Bristol-Myers to take over the development due diligence function with ImClone failed.

Clearly, with some 500 DBFs worldwide researching 1300 compounds for new biotechnology products it is no surprise that up to 30% of big pharma R&D budgets are now spent on alliances with extramural partners when the top twenty pharmaceuticals firms in 2001 spent $28 billion on intramural R&D for a yield of only 28 new drug approvals. Pfizer, currently the world's largest pharmaceuticals firm has over one thousand alliances with DBFs and universities in response to the drought. So the knowledge-based clusters and the university or research institute Centres of Excellence at their hearts continue to be the pacemakers in molecular bioscience research and rational drug design. The paper showed also how changes in funding regimes for healthcare, diminishing the traditional 'free-rider' system of clinical research in hospitals in favour of development of clinical Centres of Excellence was hastening this process. Moreover, the vast amounts of Research Council and foundation research funding for Centres of Excellence accelerates it even further. Of course, such regional clusters, drawing on national funding to meet global market demand are by no means ubiquitous. This is because, abundant though funding is, it is increasingly excellence-driven when it comes to funding allocations. Under such circumstances, alliance and partnership-based cluster governance has been shown to be an asset, and the functional presence of regional innovation systems with the full knowledge value chain in place and the lobbying and grantsmanship expertise that comes with a sophisticated science and innovation support system are invaluable.

While regions became familiar with the importance of regional innovation systems and strategies in the 1990s, the current evolutionary position in medical and biosciences research requires learning to apply those skills to creation of the infrastructure of excellence that provides the foundation for regional technological systems, which is strong and varied basic and applied research capabilities. The logic of this points to the future rise of the formulation and implementation of regional science policy. The paper asked whether there was any evidence for this. Presently, as the paper showed, there are some signs that this is indeed happening but that it sometimes arises from the sub-national, sometimes the nation-state level. Finland is a clear case of the latter, Scotland the former. Both these demographically similarly sized countries are geographically peripheral, with relatively weak market mechanisms but a strong science base. Each has developed focused science policies with

strong public funding targeted at a few world-class scientific sectors with bioscience and healthcare predominating. Elsewhere, where markets are stronger, as in the North American cases, regional governance systems capable of moving towards production of strategic science policy are either not in place, leaving an older, weaker model of piecemeal science and *technology* programmes in position. Or, like North Carolina, they are on the cusp and having moved to the kind of foresight-led, envisioning, stakeholder with action leadership process pioneered in Massachusetts, quickly adopted in Scotland (and elsewhere, e.g. Spain's Basque region; Intxaurburu & **??**) and, to some extent in Germany's regional cluster solution to its biotechnology innovation deficit, BioRegio. For the moment, the logic of this analysis implies growth of this phenomenon. This in turn means national funding bodies may have to respond by making more transparent the allocation of research funding, as demanded in Scotland's science strategy, and either devolving regional development funds or designating annual tranches for regional science development, subject always to criteria of equivalence in regard to research grants, infrastructure funding or investment in the ever developing Centres of Excellence located in regional clusters. Safeguards would be needed to prevent the target-inflation and excessive spread of investment revealed in the Finnish programmes. But equally, if regions show enterprise in mobilising scientific knowledge based bioscience or other economies, they should be appropriately awarded for so doing. Regional science policy seems likely to prove a key precondition for the fulfilment of such visions.

Acknowledgements

Thanks to Meric Gertler, Mika Kautonen, Stu Rosenfeld, David Wolfe for assistance in writing this paper.

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