Emerging Biotechnologies: Can we find out who funds R&D and what they support?

A discussion paper prepared for the Nuffield Council on Bioethics[1]

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1. Introduction

Technology and society co-evolve, mutually shaping each other. The technologies we see around us are therefore those that some elements of society or 'stakeholders' have supported. Generally these stakeholders have interests that are better advanced by particular forms of technology, perhaps in preference to other technological options that might have emerged, but were not adequately supported to do so. This raises the question of whether those technological options best suiting vested interests emerge at the expense of other, potentially more socially beneficial options. How might such biases be detected? Is it even possible to have a vantage point from where to see who funds science and technology R&D and which new technologies they are supporting? These questions, identified by the Nuffield Council on Bioethics, are addressed here.

Putting the Council's questions in context

Accounts of how technologies are socially shaped, particularly by dominant groups of actors, to the exclusion or marginalisation of others, have been a prominent theme in work by scholars studying change in socio-technical systems, from power generation to healthcare. This stream of work typically conceptualises change in variation-selection terms: stakeholder groups, or relevant actor groups generate a variety of options for change (Bijker 1995) that are then subject to a *selection environment* that differentially favours particular options (Smith et al. 2010). Change is therefore strongly constrained by pre-existing socio-technical regimes. These regimes are comprised of scientific/technical paradigms and routines that frame the thinking of actor groups (Dosi, 1982), vested interests, the organisational capital of incumbents, regulatory standards, sunk costs (Verbong and Geels 2007, Jacobsson and Johnson, 2000), practices subject to economies of scale and positive network externalities (Arthur, 1989); prevailing social practices (Shove, 2003); dominant policies, legal frameworks and professional lobbying (Walker, 2000). These constraints mean that options can be obscured and neglected, and the groups or processes influencing change may be difficult to trace, analyse and manage through policy, for example such as designing incentives to address market failures. Powerful incumbents also influence the selection environment, which maintains the momentum of established options, and creates technological lock-in and hegemonic stability (Stirling 2009, Verbong and Geels 2007). For example, if conditions or diseases can be addressed by massive investment in pharmaceutical R&D and marketing, that generates private profits, it is suggested that non-pharmaceutical solutions to addressing those conditions or diseases might not emerge or might be underutilised – a process that is part of the phenomenon described as

[1] This paper is part of an ongoing stream of research by the author. For further work see Hopkins and Siepel (forthcoming) in *Technology Analysis and Strategic Management*.

'pharmaceuticalisation' and increasingly highlighted by medical sociologists (Abraham 2011, Williams et al. 2011). Furthermore, commercial pressures (for example marketing of products even when these are less effective than other options) can lead to overuse of sub-optimal technologies (ibid). Equally, professional groups may resist some forms of technological change, for example doctors may resist use of new types of diagnostics, subsequently seen as beneficial for the care of patients (Hogarth et al. 2011).

Authors suggest that innovation pathways that result from the influence of vested interests may be suboptimal[2] or even socially undesirable (ibid, Arthur 1989, Stirling 2008, 2009). This has led to a body of research on Constructive Technology Assessment (CTA) which relies on deliberative practices such as workshops to address these problems. Yet the outcomes of the deliberative practices are quite dependent on their preparatory work, and this has been a limiting factor for CTA (Rip and Te Kulve 2008). To understand why some options are less favoured than others (e.g. wind power vs. coal for power generation) it is necessary to identify the full range of alternative options including high-tech, low tech, and organisational innovations; then identify and map out the (broadly conceived) governance regime in all its facets, to capture influences and actors; and finally work out the processes of change in an objective and symmetrical manner, i.e. study 'successful' and 'less successful' options, on the same terms (Verbong and Geels 2007). Until now such comprehensive mapping has tended to rely on historical methods (e.g. Verbong and Geels 2007). These approaches are informative, and provide rich data on socio-technical dynamics, the problems actor groups face, as well as how and when they exploit windows of opportunity. However, such approaches are necessarily retrospective and there is a question about whether they can yield results that are timely enough to inform contemporary debates.

To allow policy makers and managers to make strategic interventions to take advantage of under exploited technological options, it is necessary to find ways to gather data on patterns of R&D investment. This paper explores the feasibility of seeking data on research funding for different technological options to feed into contemporary debates and decision making. In Section 2 the paper reviews the sources of secondary data providing rapidly accessible statistics on the funding of biomedical R&D, focusing mainly on the UK, EU, and USA, as well as discussing issues related to the collection of these data and limitations in using these. Where such data does not exist in satisfactory form (e.g. data presented in too high a level of aggregation), Section 3 discusses attempts within the prior literature to generate comprehensive data on the funding of specific biomedical fields. We explore the difficulties in undertaking such studies, based on a review of some recent studies and interviews with their authors. Section 4 draws some conclusions on limitations of current efforts and puts forward suggestions for further research.

2. Sources of data on R&D funding – a brief overview

This review does not seek to provide a comprehensive analysis of existing sources providing data on biomedical funding, but rather presents illustrations of the forms in which data are available currently. The sources used provide data, compiled and presented for strategy/policy making purposes. There are other sources such as databases that would require detailed analysis from which to generate findings (e.g. patent and publication databases). We mention these briefly but are mainly concerned with readily usable resources. We distinguish between international-level work by organisations such as the OECD, commercial providers and academics, and reports by national governments and, funding agencies.

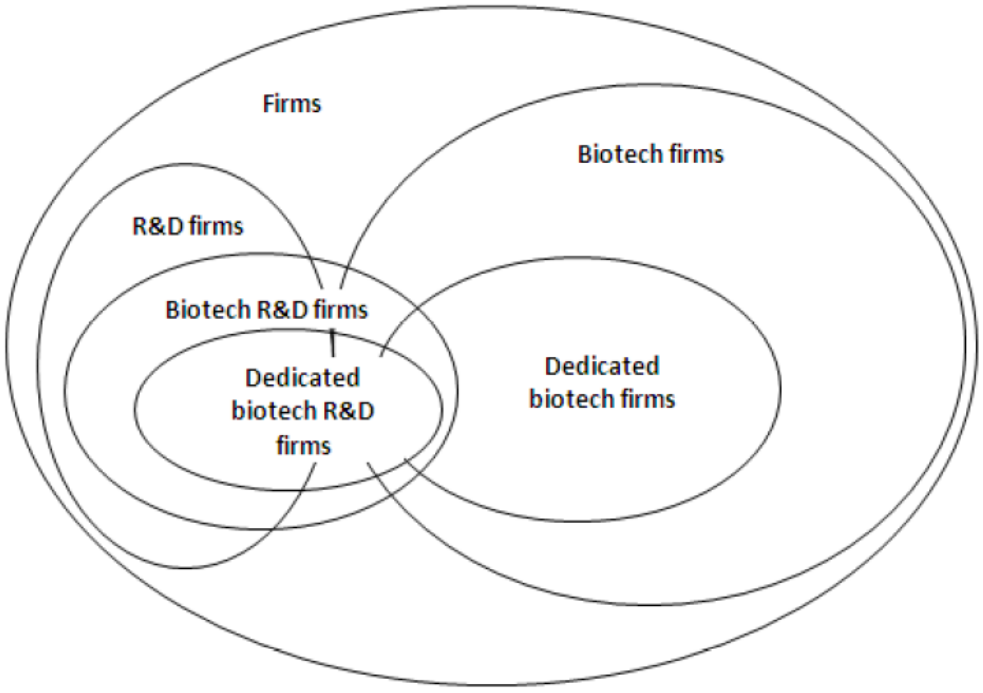
[2] While accepting Arrow's (1951) impossibility theorem - that there is no single optimal choice for all - clearly as these scholars would suggest – there will certainly be options that are worse for most than others.

At the international level, the OECD has developed a detailed statistical resource focused on 'biotechnology' for which it has established an internationally used definition:

'The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.' OECD 2005'[3]

This is a broad definition open to wide interpretation for example, application of science and technology to living organisms, might be interpreted as developing purely mechanical devices (e.g. stents) and applying these to living organisms. The OECD therefore recommends that single definitions be accompanied by lists of technical approaches that would fall within the definition (OECD 2009:9). The OECD sought to collect comparable statistics on 26 countries, but relies on surveys and data gathering generally undertaken at national level. Even basic issues such as which firms to include in surveys is complex as there are dedicated biotechnology firms that are not engaged in R&D, and firms that are apparently non-biotech focused, but that are undertaking relevant R&D activities (see Figure 1 on sample framing). This also highlights a more fundamental issue the OECD faces in distinguishing between biotechnology and traditional technologies used in pharmaceutical R&D, one of the largest users of biotechnology: What is the contribution of biotechnologies, for example tools like gene cloning, to development of pharmaceuticals? The blurring boundaries between categories of 'biotechnology' and other health-related R&D makes this more difficult to measure (OECD 2009:84). Despite these limitations the OECD Biotechnology Statistics 2009 report represents probably the most detailed and transparent attempt to gather data on the sector at the international level.

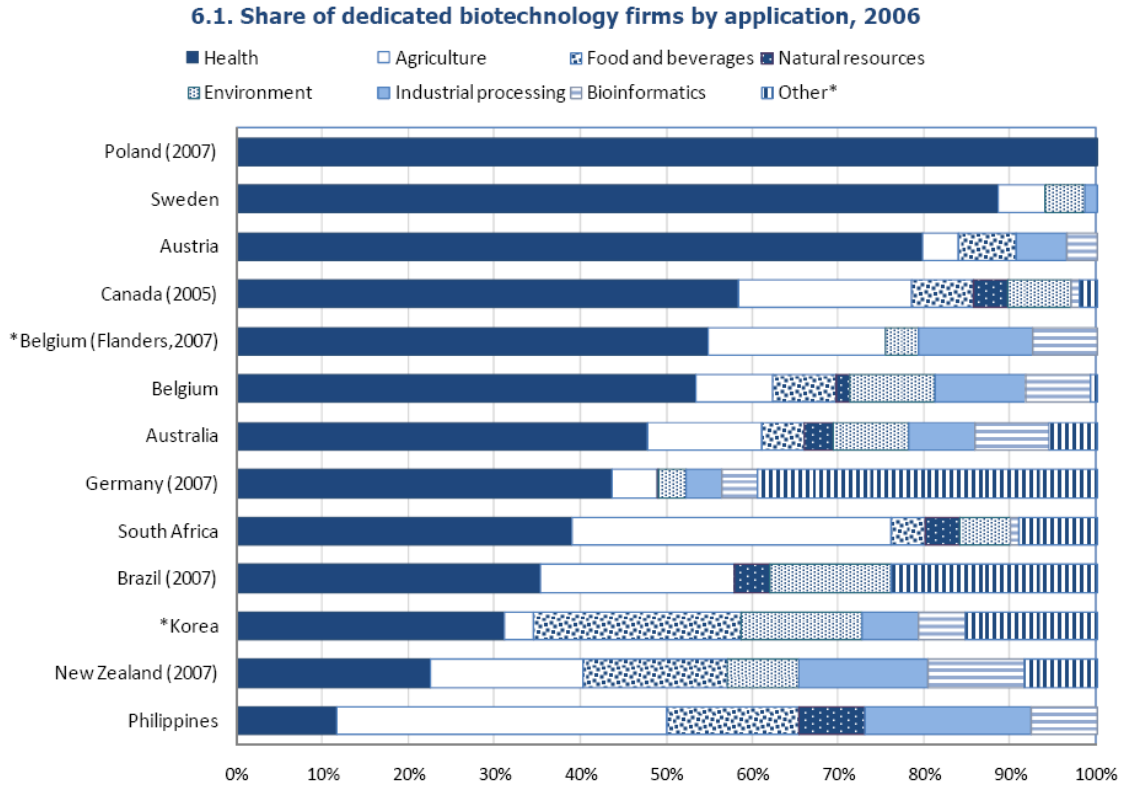
Figure 1: Sample selection - the challenge of framing surveys of Biotechnology R&D activity



Source: OECD (2009), page 10.

[3] See source here: *http://www.oecd.org/document/42/0,3746,en_2649_34537_1933994_1_1_1_1,00.html*

The OECD report reveals that definitions used and survey methods applied vary from country to country. Twenty four countries (notably excluding the UK) provided data on numbers of biotechnology firms in their national sectors, but only thirteen provided data on the industrial applications (e.g. health, agriculture, food and beverages) their firms focused on. This is sufficient to account for the sectoral focus of only 11% of expenditure in the 19 countries providing data on private R&D investments. Indeed it is difficult to even find data for the sectorial focus of dedicated biotechnology firms as the OECD's Figure 6.1, below, shows (again, note the countries NOT supplying data – major biotech centres such as the USA and UK).



Source: OECD (2009), page 57.

Data on public R&D spending seems to be even more difficult to gather and analyse for comparative purposes than for private sector R&D at the international level. Only 7 countries provided data on levels of aggregate public R&D spending on biotechnology, and these used different methods of data collection (see OECD's Table 1.2). Once again it is notable that the number of prominent biotech-supporting nations are not represented in this data. From the data available it is not possible to see which technologies within biotechnology are supported – the available data is shown below in the OECD's Table 1.2 and Figure 3.2 .

Table 1.2. Characteristics of biotechnology data sources for public biotechnology R&D

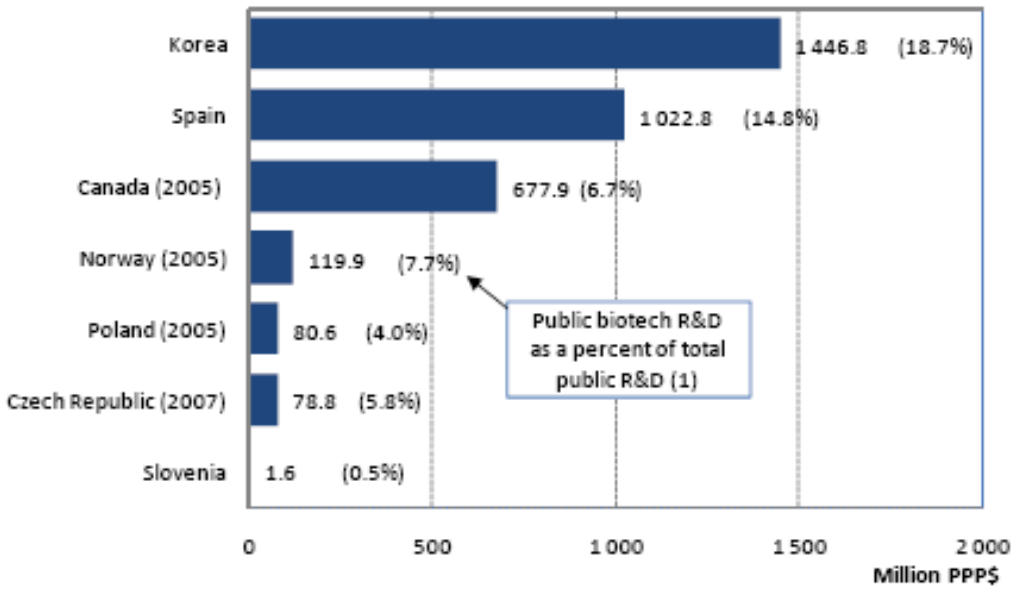
	Year	Biotech definition	Sample frame used	Extent of coverage	Mandatory	Who conducted the survey?	RR	Extra-polation
Canada	2005/2006	OECD	Census	Federal Government departments and agencies either performing Science & Technology (S&T) activities or have a budgetary allocation to fund S&T.	Yes	GOV	100%	Yes
Czech Republic	2007	OECD	R&D survey	All	Yes	GOV	88%	Partial
Korea	2006	All	R&D survey	All	No	GOV	85%	No
Norway	2005	OECD	Census	Total HES and the Norwegian Institute sector	No	NIFU STEP	90%	No
Poland	2005	OECD	Secondary sources	Selected for S&T	Yes	GOV	100%	No
Spain	2006	OECD	Census	Only government institutions with Science & Technology (S&T) activities or S&T budgets are included.	Yes	GOV	86%	No
Slovenia	2005	OECD	Secondary sources	Selected for S&T	Yes	GOV	100%	No

→ RR = Response rate; NR = Not Relevant; .. = Information not available, HES = Higher education sector.

Source: OECD, Biotechnology statistics database, January 2009.

Source: OECD (2009), p.13

3.10. Public biotechnology R&D expenditures, Million PPP$, 2006
Government and higher education biotechnology R&D



Source; OECD (2009), p.32.

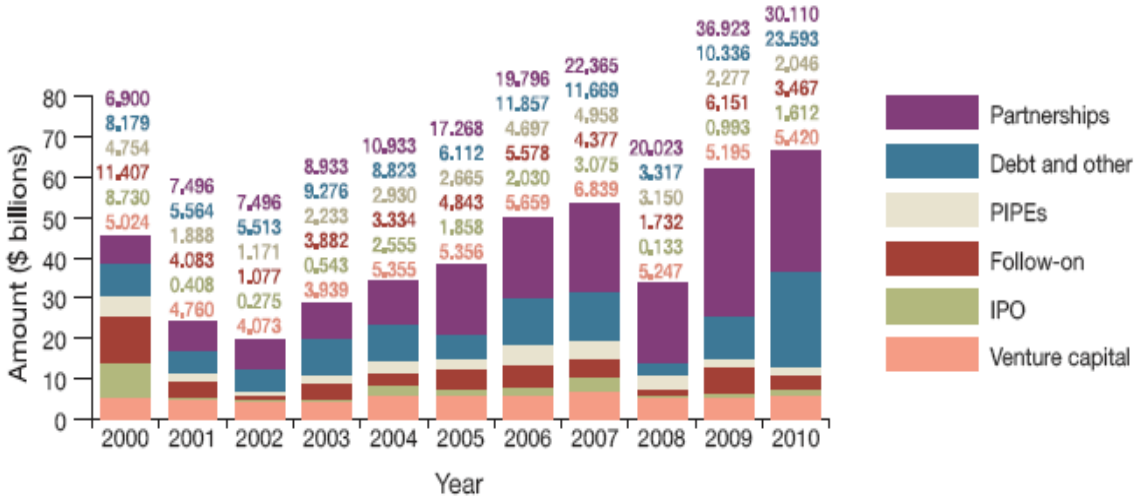
Commercial information providers such as Ernst and Young have longstanding datasets that have tracked trends in biotechnology, with an annual *Beyond Borders* report and contributions to annual reviews by journals such as *Nature Biotechnology*. Ernst and Young data is gathered and maintained by what appears to be a large team of analysts, is proprietary and, presumably, available to explore for commissioned work such as business intelligence provision. The data can be used to track the

emergence of the biotech sector (the definition here being those firms founded after the emergence of modern biotechnologies as distinct from pre-existing pharmaceutical firms). However given the blurring between the two this has become increasingly problematic from a methodological point of view. A Nature Biotechnology editorial called 'Wrong numbers' notes:

'Much if not most of the biological products and biological techniques now resides outside of the group of independent [biotech] public companies that we survey. Pharma spends $65 billion a year on R&D, 25-40% of it either devoted to biological products or using the techniques of biotech. Thus, pharma outspends 'biotech' even on biotech R&D. Furthermore biotech processes extend far beyond the pharmaceutical segment....industrial biotech for biofuels production, waste management and green chemistry.'

Leaving these criticisms aside for now, by combining Ernst and Young data with other commercial providers such as Biocentury and Recombinant Capital it is possible to collate figures for the biotech sector as a whole i.e. public and private biotech firms – still excluding the internal R&D of large pharmaceutical firms, but including work they fund externally in biotech firms – which is an increasing proportion of their R&D (Rafols et al. 2012).

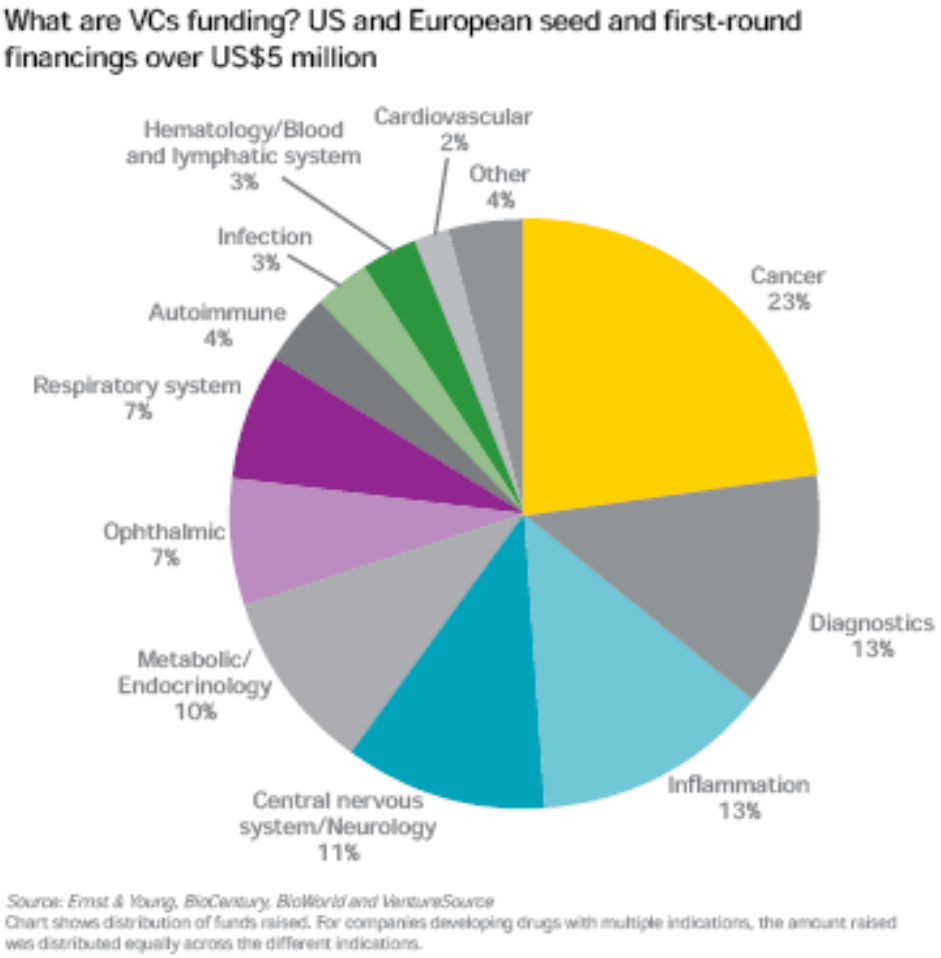
Figure 2: Total funding received by 'biotech' firms (all global data available)



Source: Huggett et al. (2011) p.585

Figure 2 shows how data gathered from different commercial databases can be compiled for what is termed the 'biotech' sector (precise definitions issues aside for a moment). The above data presumably could be divided up by the focus of the firms receiving funding, to reveal how much was going to support different technologies or disease areas as this information is often available in press releases and on company websites. However it would be resource intensive to undertake this work, and there are difficulties in reconciling financing data from different sources. For example categories for 'IPO' (initial public offering) and 'Follow-on' funding (both from stock markets) is cash firms actually receive and can invest in R&D, or indeed use for other purposes, while 'Partnerships' refers to promised money that will be paid depending on commercial progress – these are distinguished in the sector from hard cash by the term 'bio-dollars' with generally very few bio-dollars being received as real dollars because are paid against ambitious hopes of drug approvals and future sales targets.

Figure 3: What are VCs funding? Source: Ernst and Young 2011



In Figure 3, the pie chart shows the potential for displaying these commercial data on funding in a manner consistent with the aim of identifying the technological focus of commercial R&D activities to some extent. The chart show spending as split between different fields of drug development (implicit here), 'diagnostics', and 'other'. However we should bear in mind that such two dimensional data (for deals done in a single year) may be insufficient given the long incubation period of biotechnologies for healthcare and the different risk profile of early and late stage investment –ample late stage support for therapeutics may suggest sustainability of investment while a dearth of early stage funds may tell a different story in the same disease area.

Independent studies undertaken by academics can provide detailed insights into a field, but may be difficult to compile into a patchwork covering biomedicine evenly as a whole. Of course spending in pharmaceutical R&D is particularly well reported in relative terms with relatively frequent surveys of, for example, therapeutic focus or types of drugs being generated by public and private sectors internationally. Recently Pammolli et al. (2011) have undertaken a detailed longitudinal analysis of the therapeutic focus of ~18,000 therapeutic projects, highlights of which are shown in Pammolli et. al.'s Table 1. The data highlight in particular the high (and increasing) concentration of activity on cancer and could in principle be used to determine different technologies used in therapeutic R&D although this was not the focus of the paper as published.

Table 1 | **Average success rate, sales and share of the total number of R&D projects***

Anatomical Therapeutic Classification (ATC1)	Number of projects	Average sales (US$ million)	Average POS (%)	Percentage of total projects		
				1990–1999	2000–2007	Change‡
L: Antineoplastic and immunomodulating agents	6,566	105.3	1.80	21.77	29.77	+8.00
Including L01: Antineoplastic agents	5,094	92.0	1.29	16.55	23.43	+6.88
N: Nervous system	3,817	43.5	2.85	14.46	15.55	+1.09
B: Blood and blood-forming organs	822	72.9	3.81	4.11	2.38	–1.73
J: Anti-infectives for systemic use	4,737	82.4	3.92	18.85	18.41	–0.44
M: Musculoskeletal system	1,472	22.6	4.19	6.49	5.10	–1.39
A: Alimentary tract and metabolism	2,046	14.8	4.46	7.26	8.82	+1.56
R: Respiratory system	1,165	13.3	4.81	5.07	4.10	–0.97
C: Cardiovascular system	2,139	45.6	4.86	10.72	6.15	–4.57
D: Dermatologicals	859	4.4	6.64	3.63	3.13	–0.50
G: Genitourinary system and sex hormones	865	21.0	11.75	3.95	2.86	–1.09
Other (H+P+S)§	945	11.2	19.79	3.70	3.73	+0.04

Source: Pammolli et al. (2011) p.431.

At the national level, governments (and trade associations, such as PhRMA in the US, the ABPI in the UK and EFPIA at both European and national level) may compile data on biotech, life sciences, pharmaceuticals, R&D firms, and so on, and report these to support (and justify) policy making. One such recent example is work sponsored by the UK Government's Department of Business Innovation and Skills and Department of Health to support the Office of Life Sciences (itself a collaborative effort with industry). Life Sciences are recognised as being of particular economic importance within the UK and have garnered support as indicated by a series reports measuring the sector's progress in recent years. One of these notes the difficulty of the task of collating statistics on the sector:

' A fuller understanding of the UK Life Sciences market is further hampered by measurement issues as Life Sciences have not been fully and systematically included in official statistics as a separate entity. This imposes substantial difficulties in understanding impacts and contributions of Life Sciences to the economy and society more widely in the UK' BIS (2010:5).

This research has at least grasped the thorny issue of collecting data on different sectors of biomedical R&D. The most recent report (BIS 2011) produced in the series indicates that statistics are now being collected on pharmaceutical firms, medical biotechnology firms, medical technology firms and industrial biotechnology firms. Data gathered on firm numbers, employees, turnover and focus provides a detailed picture of for, example the strengths of the sector by therapeutic disease field (oncology and infection) and therapeutic technologies (small molecule drugs versus antibodies or vaccines). While only in the area of pharmaceuticals are values given for R&D spending (£4.6Bn in 2010), there is at least a detailed breakdown of the primary focus of firms in sub-sectors as show in Figure 8 and Figure 20 extracted from the BIS 2011 report, set out on the next page.

Figure 8. *Company numbers by medical technology segment in the UK*

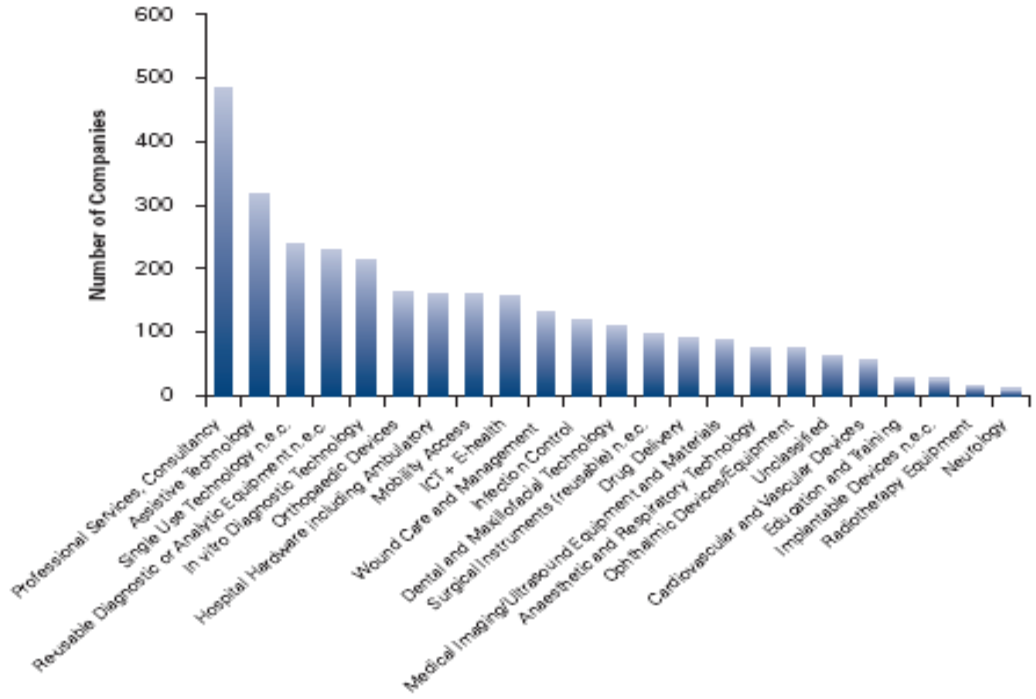
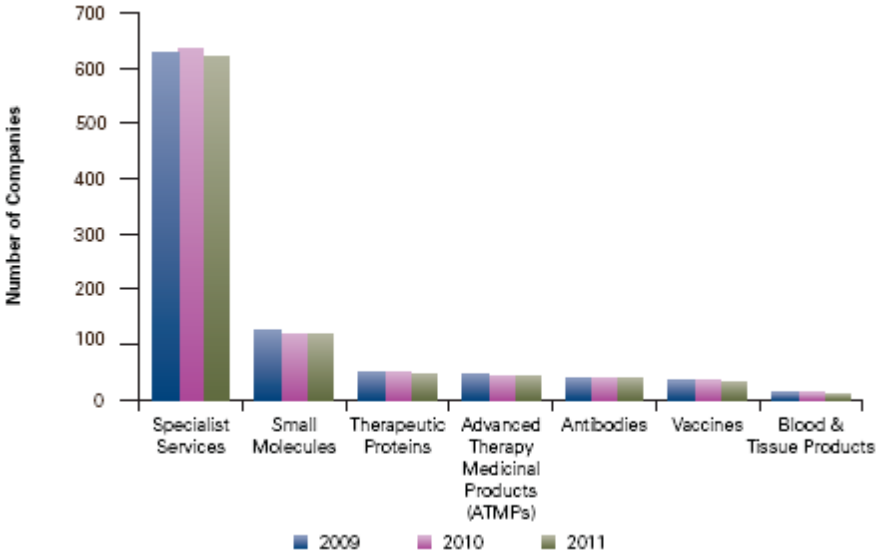


Figure 20. *Number of UK medical biotechnology companies by segment*



One limitation of the BIS reports is that public sector and charitable R&D, though mentioned, are not comprehensively analysed. Only the largest funders are identified.

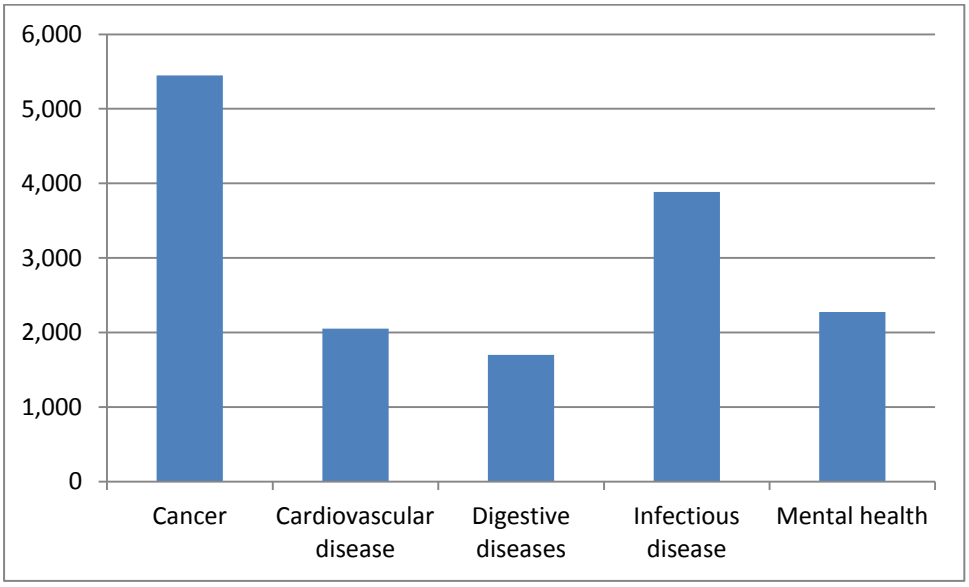
To calculate the public sector and charitable contribution to R&D within individual countries it is necessary to identify and aggregate spending by individual funding agencies. The level of transparency is highly variable with some charities such as the Wellcome Trust providing open access to lists of grants awarded and others not. Perhaps the most accessible dataset is provided by the US National Institutes of Health (NIH). The NIH distributes over $30 billion annually in research, mainly to hospitals, universities and its own laboratories. It is possible to explore the allocation of funding since 2008 using the NIH Research Portfolio Online Reporting Tools (RePORT). RePORT uses

text mining approaches applied to grant documentation to categorise funded research (in a non-mutually exclusive coding system). The system was developed at the request of the US Congress to make research spending more transparent.

However there are some limitations to the system and only data on pre-determined categories are provided. The mix of diseases, technologies and disciplines that form the current set of categories is not comprehensive and is uneven in coverage. For example while it is possible to find money spent on 'genetic testing' it is not possible to search for investments in 'diagnostics' overall. There is no category for 'pharmaceuticals' or sub-types of drugs, such as 'therapeutic monoclonal antibodies', although 'orphan drugs' have a category. There are overlapping categories for regenerative medicine and stem cells, immunization and vaccines, but none for 'medical devices'.

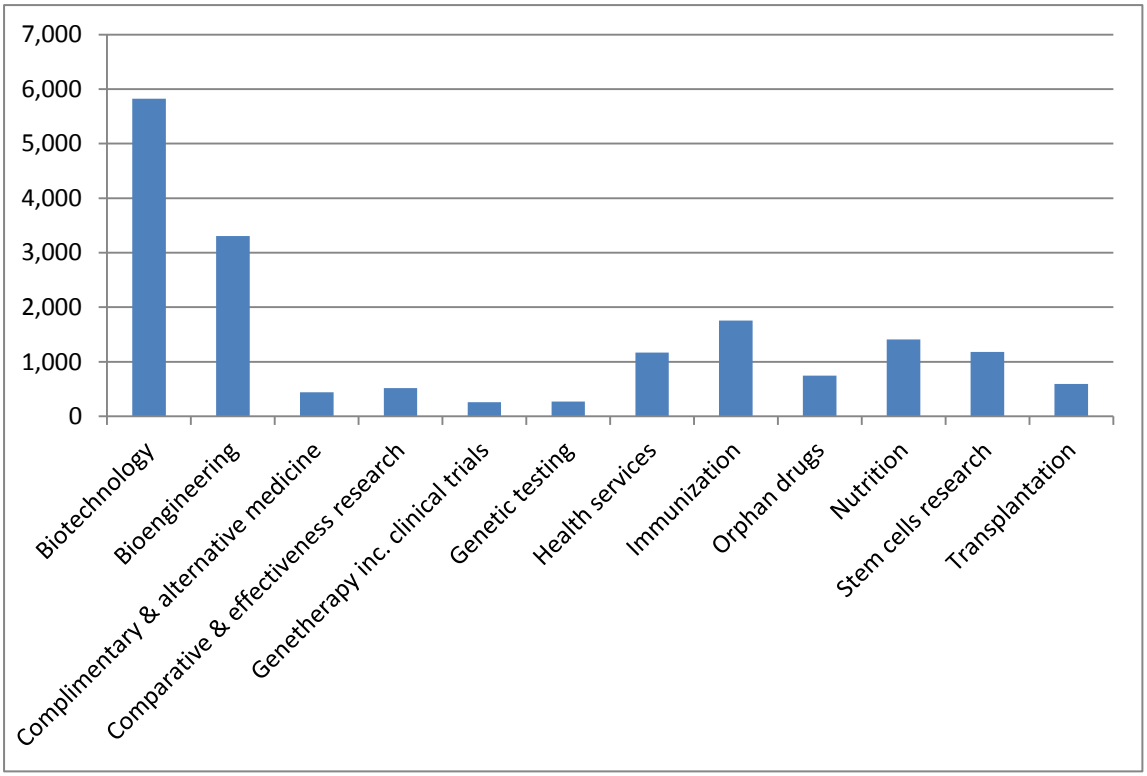
The NIH website's FAQ page on the topic of categories explains overlap and missing categories as follows: "The categories include those that were, over time, requested by Congress and other Federal agencies for reporting to Congress and the public" and notes that new categories can be requested by these groups and the categories will change over time once the system becomes more established. The categories available therefore reflect those fields that are of political interest, in broad terms, and not an analytical technological typology. Figure 4 shows a small number of relatively non-overlapping disease categories, chosen to illustrate only (but many sub-classes especially of cancer are available). Figure 4 shows levels of funding support for areas that cut across diseases including technologies and research approaches (and will therefore overlap substantially with those in Figure 5). The categories selected are more exhaustive list of those present in the RePORT category list. There is substantial duplication between categories, for example gene therapy would be entirely contained within biotechnology.

Figure 4 NIH funding ($M) in 2011 NIH in selected disease areas



Source: NIH RePORT

Figure 5: NIH funding ($m) in 2011 in selected non-disease specific fields



Source: NIH RePORT

UK research councils such as the MRC and the TSB also make information available on grants awarded going back to 2000 and 2004 respectively.[4,5] Titles, abstracts and funding amounts are available to search but unlike the NIH, there is little available analysis on aggregated levels of funding by disease area or technology focus. This would need to be undertaken by an analyst with the technical expertise necessary to develop the keyword set for each technology to be searched. The MRC has a diverse portfolio of activities and so it would be necessary to read and classify abstracts to work out if particular technologies were being supported and to what extent. However classifying abstracts for research projects by the technologies they may serve is problematic as often abstracts will not mention specific technologies and indeed may support more than one approach to dealing with a given problem, such as a disease. Box 1, containing a randomly selected abstract from an MRC funded grant provides a concrete example of the sort of information that is available on Funding bodies/ Research Council websites and illustrates the difficulty in ascribing it to a single technological option. A notable exception is the TSB, which due to its focus on technologies does contain abstracts and collections grants funded under themed competitions which can be more easily classified.

[4] http://www.technologyprogramme.org.uk/site/publicRpts/default.cfm?subcat=publicRpt1

[5] http://www.mrc.ac.uk/ResearchPortfolio/SearchPortfolio/search.htm?AdvSearch=1

Box 1: Illustrative MRC grant abstract

Adhesion receptors in the vasculature: from mouse to human

Professor S Watson, University of Birmingham

Lay Summary: This application brings together nine research groups, three of which are headed by clinicians, to investigate various aspects of the blood vasculature in health and disease. Each group has expertise in distinct but complementary areas of research and bringing them together through the formation of an MRC co-operative group has several advantages including (i) added value that will come from closer interactions and shared expertise within the co-operative group; (ii) a reduction in research costs through sharing of materials and equipment; and, most importantly, (iii) the opportunity to take on more complex scientific problems. The co-operative will focus on vascular diseases including atherosclerosis, thrombosis and the generation of new blood vessels in cancer and tissue repair. In addition the role of the vasculature in inflammatory disease will be studied in the context of direct damage to blood vessels (vasculitis) or conditions where inflammation occurs in tissues as a consequence of inappropriate recruitment of inflammatory cells from the blood (inflammatory liver disease and rheumatoid arthritis). These diseases are all caused by defects in the same types of vascular cells including white blood cells, endothelial cells (which line the blood vessel) and platelets. Thus, the knowledge of one research group in the role of a particular disease or cell type will be readily applicable to that of another. The bringing together of clinically-based and basic research groups with complementary expertise in related areas will enable us to define the molecular mechanisms of vascular physiology and pathology and thereby to provide important new insights into disease processes which are a major health burden on society.

Scientific Abstract: This is a request to establish an MRC Co-operative Group at the University of Birmingham to investigate the role of adhesion molecules and their receptors within the vasculature in health and disease. The co-operative will be made up of three clinical groups with active research laboratories and six basic science groups with expertise in a variety of vascular cells including endothelial cells, haematopoietic cell precursors, fibroblasts, lymphocytes, mast cells, megakaryocytes, neutrophils, platelets and smooth muscle. Seven of these groups already have a strong track record of collaboration and interaction in Birmingham and have played a major role in establishing an international reputation for the University in the field of adhesion events in the vasculature. The arrival of Watson and Frampton from Oxford builds on this by bringing skills in mouse genetics, a strengthening of intracellular signalling and provision of complementary expertise in platelets and thrombosis. Eight of these groups, and part of the ninth group, will relocate to two new research facilities, the Institute of Biomedical Research (IBR) and the adjacent Cardiovascular Link Building (CLB), in the autumn of 2003 thereby providing a further impetus to the formation of the co-operative grouping. Several of the members of the co-operative are also part of The MRC Centre for Immune Regulation which will move to the IBR at this time. The theme of this application is highly complementary to the work of the MRC Centre and both groups will benefit from their close proximity and overlapping interests.

The different sources of readily available data reviewed above have a number of limitations that make them individually and collectively insufficient to address the questions posed in Section 1. These include varying definitions of technology, insufficient categorisation, or a focus on disease – rather than technology, difficulties in accessing data, inconsistencies and gaps in data collection. This raises concerns as an Editorial in *Nature Biotechnology* concludes:

'To quantify innovation, we need to look too at activities within small private companies and, increasingly, at the early translational work in the public sector. These data are exponentially more difficult to gather than data from publicly quoted firms. Accordingly, policy makers, governments and industry associations need to devote much more effort and resources to collecting them.' (Editorial, Nature Biotechnology 2010:761).

However while this may be encouraged, data gathered for policymaking over periods of time are problematic. The purpose determines who collects the data, and who contributes, how much care they take, the form in which data is sought, where it is found, how it is counted or excluded, aggregated or partitioned, unitised, coded, tabulated, stored, analysed and presented. Each step further separates the reader from the phenomena being observed – which change as a result of

being observed – particularly where funding is involved. For example, Calvert (2006) observes how projects can shift between definitions of 'basic' or 'applied' research or from one subject to another according to research funding policy.

Section 3 - What can input-output studies tell us about tracking R&D investments?

In Section 3 we consider how a more comprehensive approach to tracking R&D support for different technologies might be developed and anticipate the difficulties such an approach might face. In undertaking this approach, a number of prior studies and their authors have been consulted (see Table 2 below). These mostly form part of what might be described as 'input-output' analyses that look at qualitative or quantitative socio-economic returns from R&D money spent in biotech or health research. This appears to be a relatively recent body of research and one where robust methods are still under development (HERG/OHE/RAND Europe 2008). Inputs are measured as R&D funding and outputs, measured some time later (perhaps 15 or even 20 years, due to the lag in medical innovations generating payoffs) using metrics such as either lives saved, Quality Adjusted Life Years (QUALYs) gained (ibid), or even revenues generated by economic spill-over effects such as job creation (Battelle 2011). These models have been used to justify the financing of health research, but some of them have also been criticised for their simplistic methods (e.g. Drake 2011).

The reason for drawing on these studies here is not that they provide input-output analysis, but because to undertake such analysis, authors first make a careful search for inputs in a specific field or fields. It is this feature of their method they share in common with the method that would be required to address the questions posed above in Section 1. In highlighting the difficulties in undertaking these studies, *the following discussion is in no way a criticism* of the authors of these reports or of scientific or policy value of the reports themselves – all of which contain explicit caveats on the analysis they provide. Instead, this discussion seeks to highlight the difficulties that any study attempting to quantify financial R&D inputs would encounter. The views expressed by the interviewees, and this author are therefore intended as general statements about these kinds of searches, and not the validity of particular studies.

Table 2: Reports analysed and authors interviewed

Report	Topic	Interviewee(s)
Office of Health Economics (2012 forthcoming) 'The cost of a new medicine'	Estimating the cost per successful drug discovery R&D project	Jon Sussex (JS), Jorge Mestre-Ferrandiz (JMF), Office of Health Economics
Molly Morgan Jones and Jonathan Grant (2011) 'Complex trauma research in the UK' RAND Europe	An analysis of the funding sources, research priorities and capabilities in the field of complex trauma in the year 2008/2009.	Molly Morgan Jones (MMJ), RAND Europe
Health Economics Research Group, Office of Health Economics, RAND Europe (2008) Medical research: What is it worth? Estimating the economic benefits from medical research in the UK. London: UK evaluation forum.	Estimating the economic returns from public and private R&D investments in the UK in cardiovascular disease and mental health.	Jon Sussex (JS), Jorge Mestre-Ferrandiz (JMF) , Office of Health Economics
C. Enzing et al. (2007) BioPolis: Inventory and analysis of national public policies that stimulate biotechnology research, its exploitation and commercialisation by industry in Europe in the period 2002–2005: Brussels, European Commission.	An analysis of the funding and wider policy environment for biotechnology in 28 European countries spanning at the deepest level of analysis (for a subset of 18) the impact of funding made in the period 2002-2005.	Ismael Rafols (IR) SPRU, University of Sussex

To address the Council's questions from Section 1 it is necessary to identify as completely as possible: (i) The funding organisations supporting a given area (across public/ private/ charity sectors) and (ii) the technological options that they invest in, within clearly delineated fields (e.g. cardiovascular disease) and funding volumes (research spend) over time. These are explored in turn below.

(i) Finding the bodies that fund R&D

The key starting point is deciding where to look for finance for R&D inputs. Studies sponsored at a national level may focus on national institutions, but a national innovation system may benefit from international inputs at multiple points, such as research grants and multinational corporate R&D (Enzing et al. 2008). However in practice studies have not tracked international influences as Jon Sussex (JS) at OHE notes:

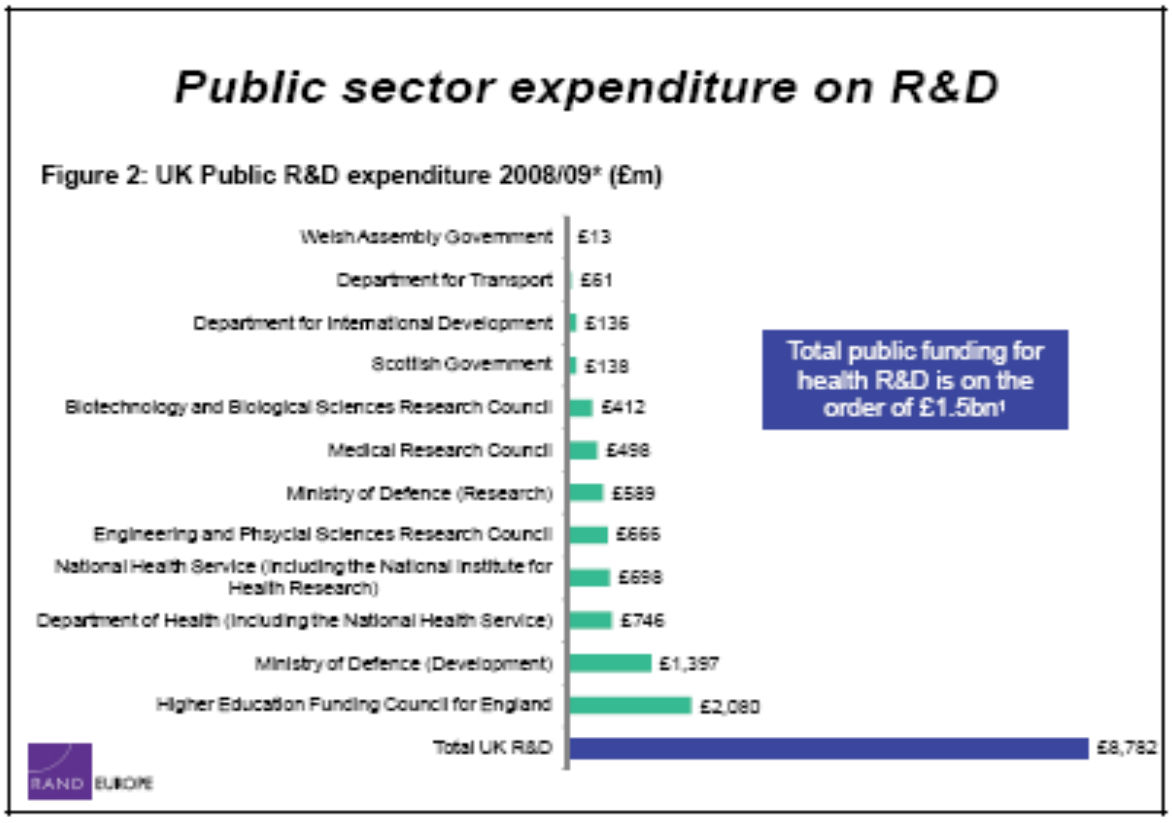
"in terms of research outcomes it is actually impossible to take into account international influence....we all recognise that it is there but I am not aware of anyone taking [it] into account....

other than assuming it away [i.e.] just looking at the US and saying let's assume the US equals the world because it is a dominant player in medical research and a very large economy by itself". As JS notes this is an even less meaningful or desirable assumption for smaller countries "The UK does not equal the world so you can't get away with that here".

One key factor contributing to the "impossibility" of the task is presumably the large number of organisations that might be funding research and how to know which ones to approach for data. A further complication is that organisations do not map onto technological or disease fields neatly as few organisations in biotech or biomedicine have a single focus, so without working backwards from a given field such as a disease, we do not know *a priori* which organisations to include in the exercise.

Molly Morgan Jones (MMJ) at RAND Europe undertook a study for the UK Department of Health to identify funders supporting the relatively small field of complex trauma, having initially identified the main funders of UK public-sector R&D (see Figure 6). This was achieved by first undertaking interviews with scientists in the field and then a bibliometric analysis, using key words, to identify publications in the field to track authors of relevant research and finally find out who had funded this work. The need to find funding support mechanisms within government departments, at national and regional levels, as well as charitable and large and small private firms makes this time consuming. For example even though complex trauma is a small field (receiving perhaps £15M per year) and only funding in a single financial year was recorded, the exercise out took several weeks of research. Similarly for the Biopolis project Ismael Rafols (IR) reports that gathering such data for public sector spending on biotechnology took months per country, even for small European countries, and the reliability of the data was uncertain.

Figure6: UK Public sector research expenditure on R&D



Source: Morgan Jones and Grant (2011) page 8.

(ii) Which technological options do funders invest in, and how much do they spend over time?

With some time, it is possible to collate information at the national level for total R&D spend in key sectors such as healthcare because ministries, departments, charities, firms, their subsidiaries or divisions may be split along such lines. For example Morgan Jones and Grant (2011) were able to report that total UK public sector spending on health related R&D was £1.5Bn in 2008/2009, while biomedical charities spent £1.1Bn, and private industry invested £8.9Bn. However identification of spending on sub-fields or technologies is more difficult.

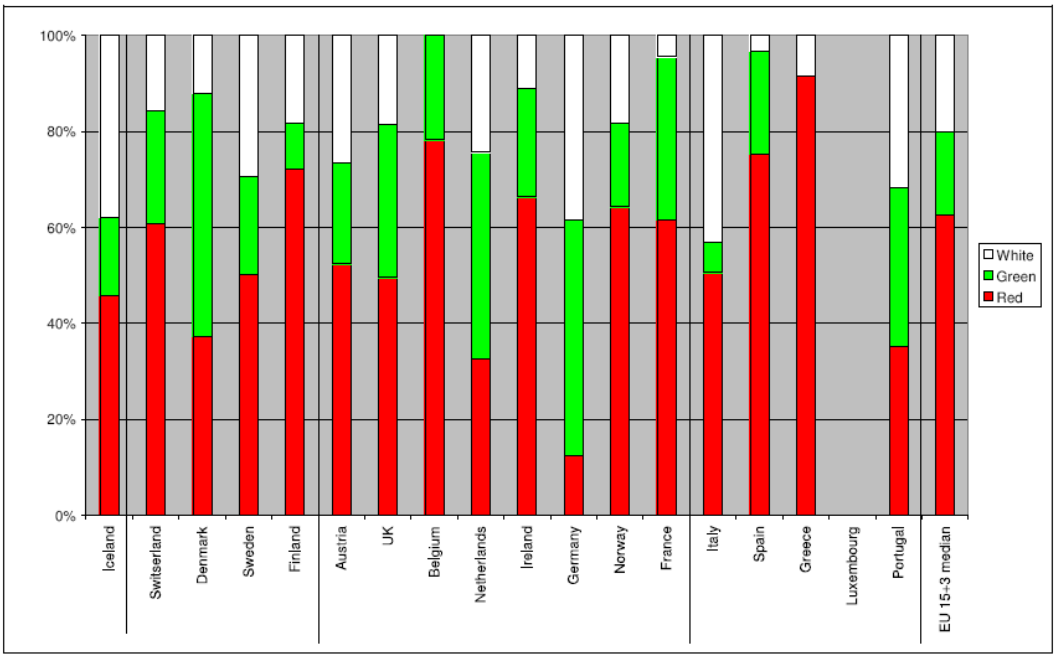
As identified in Section 2, the scope of data collected is determined by the definition of the field as established by the analyst, but this may not match with their secondary sources and the R&D funders themselves. This data has to be discussed and collected through an interactive process with funders – who may or may not devote their time to helping with such enquiries.

Research teams (and their clients) may develop definitions of the field that reflect their own perceptions or interests in the field to be studied and therefore are not recognised by those they approach for data or do not reflect they way in which these organisations gather their own data.

IR recalled large differences in the response rates in different countries to invitations to contribute to research studies (similarly experienced by the OECD as shown in Section 2), an immediate impediment to understanding how funding is invested. However where there was support, IR used correspondence with a national agency funding biotechnology R&D to illustrate how even very helpful respondents could only provide very limited useful information even when the aim of the research was to classify biotechnology investments into broad sectors of application: "She doesn't use our categories, we don't use hers" he concluded. Others were less helpful when completing survey forms, IR recalls: "Most respondents leave empty the specifications of percentage allocated to different funding categories by application areas covered and activities" although he noted they could qualitatively distinguish the goals, such as 'firm creation', and activities their funding aimed to support, e.g. whether the funding was meant for applied or basic research. JS similarly noted that some research funders focused more on the types of things funded (buildings, research, numbers of people) than technologies and their accounting methods reflected this.

While some data can be gained on funding priorities at the national level, this is likely to be incomplete and charts (such as Biopolis' Figure 4.10 below) may be misinterpreted if taken out of context (i.e. that only some data is available). For the purposes of addressing our question of how different technological options have been supported, the data below is unhelpful, being focused on sub-sectors only (red, green and white biotechnology).

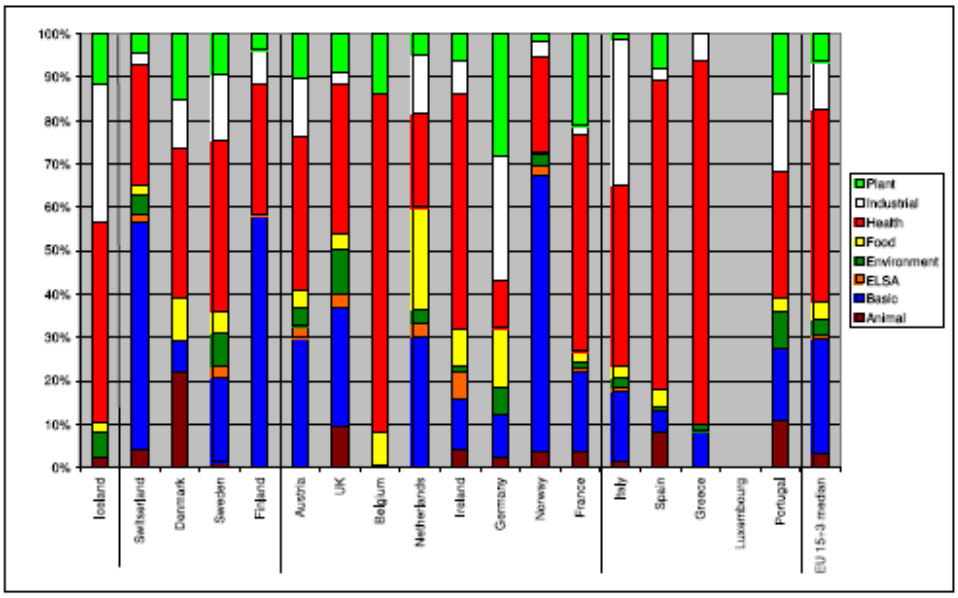
Figure 4.10 Public funding of biotechnology in three main application areas in the EU15+3 countries, in M PPP$, 2002-2005[15]



Source: BioPolis Research

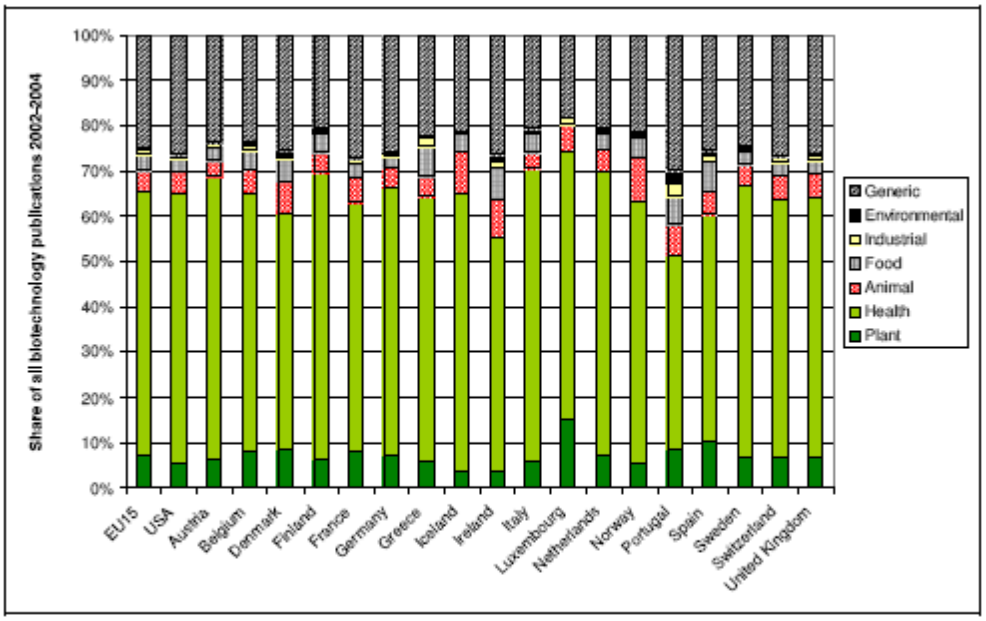
Biopolis' Figure 4.11 introduces further complexity to the picture by allowing funders to specify if their funding was for applied research areas or basic research (which as noted by Calvert 2006 is a difficult distinction in practice). Figure 4.11 provides an interesting contrast with Figure 4.12, which draws on output measures of biotechnology competency using classification of publications. What would appear to be quite different funding priorities (Figure 4.11) seem not to have much of an impact on the proportion of publications produced by the national science base, perhaps reflecting that a large proportion of research that is undertaken is not dependent on the focus of the funding schemes reporting data to the Biopolis project (although this disparity is open to a number of interpretations – another being that centrally coded and indexed databases on publications, in Figure 4.12 are more standardised and consistent than funding categorised by survey contributors at the national level shown in Figure 4.11).

Figure 4.11 Share of biotechnology application areas in public funding in the EU15+3 countries, 2002-2005[16]



Source: BioPolis Research

Figure 4.12 Specialisation patterns of EU15+3 in sub-areas of biotechnology



The figure shows the ratio of publications in subfields of biotechnology to all biotechnology publications for the period 2002-2004

Source: BioPolis Research

All those interviewed discussed how the most transparent of research funders, particularly large charities and UK research councils provided lists of projects that had been funded each year but that classifying these into disease areas or technological fields was problematic. Firstly, technical expertise is often needed to avoid making mistakes, and secondly the information available (such as a project title or abstract) may be insufficient to make judgements on as noted in Section 2. Finally, some projects particularly at the most basic research such as identifying disease mechanisms, may be so generic that it could be seen as relevant to several different avenues of research (see Box 1 in

Section 2). See RAND's Table 2 (below) illustrating how project titles may be coded by analyst's categorisation.

Table 2: MRC projects in the area of complex trauma research

Project title	Amount	Years	Institution	Trauma area
Neuro-inflammation following human traumatic brain injury	£205,220	2009–12	University of Cambridge	Acute injury
Novel non-invasive optical methods to characterise cerebral oxygen delivery and utilisation after traumatic brain injury	£295,297	2009–11	University College London	Acute injury
RESCUEicp decompressive craniectomy study	£877,384	2008–13	University of Cambridge	Acute injury
Overcoming the limitations of allograft in impaction bone grafting for revision arthroplasty	£462,159	2010–12	University of Southampton	Regenerative medicine
Mechanical cardioversion: basic principles and clinical utility	£340,349	2005–09	University of Oxford	Acute injury: resuscitation
Mechanisms of interleukin-1 action in neuronal injury	£754,131	2009–12	University of Manchester	Acute injury
Novel bio-synthetic matrix for ocular surface reconstruction	£91,311	2008–09	University of Nottingham	Acute injury: peripheral nerve injury
Promoting plasticity and repair after spinal cord injury	£619,462	2003–11	King's College London	Regenerative medicine: plastic and reconstructive surgery
DAVROS: development and validation of risk-adjusted outcomes for systems of emergency medical care	£951,517	2007–11	University of Sheffield	Medical training: simulation Acute injury: decision support

Source: RAND Europe 2011. p.16

So far we have focused on the collation of data on public funding but is it possible to track private firms' investment in specific technologies? Yes – on occasion. In biomedicine particular firms are founded with a focus on a particular technology, and indeed if these firms are successful in bringing a product to market or even if they are bought by a larger firm they may present a good opportunity to isolate the finances put into that technology. However, these firms are typically small. For example Hopkins et al. (2013) use a dataset of all UK therapeutic biotech firms to shows that in the 22 years prior to 2010 all the publicly listed therapeutic SMEs raised less capital than GSK made in profit in 2009). They also may not be the sole supporters of a given technological option. Therefore the prime question becomes, *is it possible to track technological investments of large firms*? Indeed, private sector data on large firms' investments by technology are also difficult to collect, as Jorge Mestre-Ferrandiz (JMF) recalled:

"it is always difficult for firms to work out what they are spending per specific technology in preclinical work because their investment is not technology specific even if you have access [to the interviewees]. Following clinical trials (phase I,II and III) is more tractable, more manageable"

This illustrates how in some areas firms can provide data, but not in others. In one study JMF had asked pharmaceutical firms to estimate their spending on orphan drugs:

"they told us it would be difficult to disentangle that information internally, they wouldn't recognise what was orphan and non-orphan... they didn't know how to apportion it internally".

This is a reflection not of secrecy, JS maintained, but of the motivation for collecting the data in the first place as he explained:

"if they [big pharma firm X] have a research facility at [town Y] all they need to know is how much it costs to keep going. Sometimes those facilities coincide with projects in individual groups of technology or individual technologies if you are lucky but most of the time they don't. They never actually have the information in the form you need it for the type of [report] you are talking about."

Even where data had been collected in relation to specific fields (diseases or technologies) it was also highlighted as subject to recall bias and changes in the way data might be classified at different points in time.

MMJ noted "research can be its own beast – you might find something different than you set out to find...look at anti-retroviral drugs for HIV/AIDs, they were a failed cancer drug" hence the expenditure might have been recorded differently depending on when an analyst had asked what the money was spent on that first generated that drug. JS made a similar point:

"....there is a difference in the ex-ante and the ex-post view. Ex-post you say this is what we produced and everything we spent on R&D produced this...Ex-ante you may think you were spending on a whole range of stuff most of which never made it to the market."

For these reasons, tracking firm's investment in R&D is best undertaken using data based on historical sources, but this requires access to data over many years. Such data is available if a proxy, such as looking at projects rather than sums of money invested is used, but this may not be applicable for all technologies. For example as the Pammolli et al. (2011) study indicates, pharmaceuticals are well addressed using this measure, but other technologies (e.g. diagnostics) less so.

Can a study to track technological options be designed? Initial interviewee responses

In moving beyond discussions of prior studies towards advice on whether funding for specific technological options could be tracked, interviewees responded with a range of pragmatic views emphasising resource intensiveness and the limitations of results:

JMF: “it is doable but it won’t be perfect... that is for sure... it is labour intensive”

MMJ: “I think it would be a big study. I think you would need a lot of hands on deck...I would suggest a small scoping study of a small area first a particular disease area maybe.”

However JS had a contrasting view – as he felt that a lot of the money spent on research could not be related to specific technological trajectories but rather contributed to maintaining the absorptive capacity of the science base. This means that when a good idea came along it could be exploited successfully as there was capability present to develop it. Therefore narrow studies of technological options would be misrepresentative in his view as they would likely not pick up spillover effects that trajectories benefitted from or to which they contributed. Instead he recommended top down studies of large fields where these spillovers could be captured.

IR on the other hand suggested that the use of proxy measures of activity captured from research outcomes (such as publications or patents) may be more reliable to track intensity of research than top down approaches such expenditure reporting. Since each of these proxies is sensitive to bias, various measures should ideally be combined to reveal different characteristics of technological trajectories. For example Searls and Agarwal (2009) have successfully used publications, and Pammolli et al. (2011) number of pharmaceutical projects, to estimate efforts in a certain area of disease at a global level. MMJ also notes the importance of using multiple approaches and sources as a robustness check.

4. Conclusions

The development of policies and strategies to address biases in resource allocation caused by vested interests or market failure and to exploit neglected emerging technological options depends on the availability of data to guide decision making. We have sought to find out whether it is feasible to gather data on R&D funding to map how different technological options are supported.

Using primary and secondary accounts of data collection efforts it is clear that a substantial number of hurdles would need to be overcome to gather data on which organisations are investing in different forms of technology. This is particularly difficult when we consider that technologies may develop on a global stage and so the search for their supporters must also be global, and the support of many different groups may be necessary to collect standardised data. This is likely to be very resource intensive, but not impossible. Some key issues related to the difficulties in utilising existing sources of data (with specific illustrative examples) are summarised in Table 3 below and provide lessons that would be helpful in guiding data collection.

Table 3: Key sources of data analysed and their utility for assessing technological options

Sources	Type of data	Limitation of utility for identifying funding of technology options
OECD statistics (illustrative of NGO international data collections)	Wide range of statistics for Biotech investment by public and private sectors, including numbers of firms active in sector and total R&D investments by sub-sector.	Variable and incomplete responses across countries, differences in methods and definitions used. Focuses on disease categories and has insufficient classification of individual technologies
Ernst and Young, BioCentury, Nature Biotechnology (illustrative of commercial data collections)	Global data gathered annually particularly focused on funding sources such as VC and Stock markets.	Useful for capturing data on investment in public companies, but funding from corporate alliances is a large component, subject to over estimation of funding due to commercial sensitivity of contracts agreed. Data on technology focus is not available without commissioning, and would be subject to limitations of classification (as detailed in Section 3).
Pammolli et al. (2011) (illustrative of academic data collections)	Published study of global pharmaceuticals R&D pipeline based on proprietary dataset of drug development projects	By focusing on drug projects (which can be characterised in detail, based on public disclosures by company and proprietary data) proxy measures of firm disease area focus can be obtained. The emphasis firms place on certain technologies, e.g. RNAi therapeutics, or Monoclonal anti-body therapeutics, would also be discernible with additional work.
BIS (2011) (Illustrative of national statistics gathered on an industrial sector)	Dedicated collection of data on the UK 'Life Science Industry', with data on *inter alia* R&D investment, firm focus, employee numbers, earnings, geographic location.	This is an attempt to gather comprehensive data at the national level. While firms are classified according to their focus in some detail, there is no detailed assessment of which technologies are being invested in.
NIH (illustrative of a well indexed database of publicly funded grants)	Database of grants funded (since 1988). Data can be readily downloaded for analysis and titles and abstracts and are searchable by key word. Funding amounts are recorded.	Overview statistics are provided to address requests by US Congress but categories are generally disease-focused rather than technology focused and categorisation system is uneven with some key technologies uncategorised (e.g. synthetic chemical drugs, Humanised antibodies).
TSB (illustrative of an un-indexed database of publicly funded grants on technology)	Information on grants funded since 2004, including titles, abstracts and funding amounts. Searchable by key word.	Grants are focused on supporting technologies, generally these are themed programmatically. This makes identification of technologies relatively straightforward.
MRC (illustrative of an un-indexed database of publicly funded grants on science.	Information on grants funded since 2004, including authors, titles, abstracts and funding amounts. Searchable by key word.	Grants are often not worded in a manner that emphasises technological application, especially when the focus of research is fundamental understanding, e.g. of disease processes.

The findings from reviewing these sources suggest that at least in some countries such as the USA and UK there is increasingly transparency over who is winning public sector grants, and what the subject matter of the research is. However it is more difficult to aggregate funding across a range of grants to work out how much money is being invested in specific technologies, either because these technologies are not named in the abstracts or because grants support fundamental research which may support multiple technological options.

This suggests that analysts will need to develop their own classifications systems if the central task this paper addresses is to be undertaken. Caution is urged though to ensure classification systems interpret technology as being composed not just of artefacts (drugs, devices) but techniques and also regimes (rules, regulations, guidelines) that may not be counted as innovations (Hopkins 2004, 2006, NESTA 2006), but which can be very important economically – the link between smoking and cancer and resulting public health interventions aimed at smoking cessation being a prime example (HERG/OHE/RAND 2008).

Perhaps of more fundamental concern, differences in *inter alia,* definitions, accounting procedures, priorities, recall, and judgement all pose more difficult (from a pragmatic point of view) barriers to accurately recording investment in particular technological options across a wide number of organisations. In part this is due to differences in the mission of government, charities and firms, but it is also due to fundamental problems such as survival bias in projects (forgotten failures) and spillover effects whereby spending in one technological option feeds into advances in another.

Fortunately we need not divide up R&D spending into precise sub-fields to draw some important conclusions on the social shaping of technologies by stakeholders, particularly in healthcare and related life sciences, because essentially there is an elephant in the room. Perhaps the clearest indication of potential for bias in the support of particular technological trajectories comes from the observation by Morgan Jones and Grant (2011) that total UK public sector spending on health related R&D was £1.5Bn in 2008/2009, while biomedical charities spent £1.1Bn, and private industry invested £8.9Bn. Thus, UK industry outspends the combined public and not-for-profit sectors by more than three times, and this impact is further accentuated because industry is likely to spend a greater share of its more considerable resource on later stage development than earlier stage research (Jensen, 2010).[6] In other words, the public sector may open many avenues, but private firms will select which are exploited and the private firms with the most spending power are pharmaceutical firms. Furthermore as Jon Sussex notes in Section 3, influence in the shaping of technologies is not merely national. Globally the pharmaceutical industry is estimated to spend $150 billion[7] on pharmaceutical R&D annually (Munos 2011) a sum that is likely to significantly bias the development of biomedical technologies towards pharmaceutical solutions, rather than say behavioural interventions.

The question of whether it is possible to identify how different technological options are financially supported therefore becomes primarily a question of whether it is possible to track the R&D expenditures of a relatively few large pharmaceutical firms (the top 15 US/EU firms spent three times more in R&D in 2009 than the NIH for example – Rafols et al. 2012).

The evidence gathered in Section 3 suggests that large firms typically do not structure their accounts to track investments by technological option, but more likely by R&D site, country and perhaps in the case of expensive late stage clinical products, development programmes will have their own budgets. Therefore attempts to track technological options using data on funding inputs may rapidly become 'pharmaceuticalised' as the costs of such studies may well be the most significant feature of R&D spend, while pharmaceutical drugs remain much more visible forms of biomedical innovation than many others, such as diagnostics, devices or health services.

This suggests that the use of proxy-measures as signals of R&D activity may be more practical than seeking to collect financing data. Proxy-measures, particularly patents and publications have certain

[6] http://sciencecareers.sciencemag.org/career_magazine/previous_issues/articles/2010_12_17/caredit.a1000122 [Accessed February 21, 2012].

[7] Cf. The quote from Nature Biotech for 'big pharma' spending $65bn in R&D. Munos' broader scope explains the wide disparity.

advantages in biomedical innovation. For example public databases are widely available at little or no cost, and the data on these are carefully indexed over long periods of time (although there are differences over time in coverage that require adjustment). These can be also be retrospectively interrogated using different keywords or classifications and without being subject to the sorts of recall bias individuals and organisations suffer from. Of course these proxy measures are not a panacea, and hence sets of different measures may have to be used.

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