Innovation Processes in Genomics Industry Sectors

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Brief Background/Aims of the Project

Genomics-based innovation is fundamentally restructuring the nature of traditional scientific research, and its commercial utility, in both public and private sector organisations. Evidence for this can be observed through the complex re-alignments that are taking place in the pharmaceutical and agro-biotechnology sectors, and the evolving, as well as devolving, networks that are beginning to define and shape new relationships within and between companies. Interactions between relevant actors (scientists, managers, policymakers etc) are also becoming increasingly volatile, and the traditional relationship between product discovery and marketing is undergoing profound change. The primary aim of this project is to explore the nature, direction and management of innovation processes in the pharmaceutical and agro-biotechnology sectors, and generate greater understanding of the complex and diverse strategies employed by various actors within these sectors as they attempt to both direct the trajectory of the science and technology, as well as mould the regulatory/policy environment in such a way that a vibrant commercial market can be sustained. The purpose of this position paper will be to set out some of the broader substantive theoretical and empirical issues relevant to this project, and elucidate some preliminary research strategies. A very broad literature will be critically evaluated. The paper will begin by enumerating a number of relevant theoretical and empirical issues and questions that may provide useful foci for the research. (This paper will concentrate predominantly on the pharmaceutical industry, although the general project will also include analysis of the agro-biotech sector and its various value chains) Next, some of the normative issues will be discussed in greater detail. Finally, a short summary of the methodological approaches that will be used to explore these issues will be provided.

Brief Overview of the Sectors

Dramatic changes have taken place in the pharmaceutical/healthcare sectors over the past twenty years. Several key factors, according to a Wood Mackenzie report (PharmaForum, no. 45, 2000) have contributed to the unprecedented rate of growth in the industry. Firstly, ageing populations and higher life expectancy in the developed world has fuelled increasing demand for innovative drugs. The growing success of emerging economies has also raised demand for pharmaceutical products in hitherto untapped markets. Secondly, consumer demand, particularly in the United States, has been fuelled by ever more innovative marketing techniques, particularly direct to consumer advertising. Thirdly, the discovery and development of novel genomics-based
The unprecedented growth in our knowledge of genomics is fundamentally reshaping the pharmaceutical and agro-biotech industry landscape. During the 1980s and 1990s, these two divergent industries began to integrate their R&D expertise. The underlying rationale was that both sectors could profit immensely from the adoption of a “life science” paradigm, and that at the early stages of R&D, in particular, a synergetic approach would offer the most apposite strategy. The consequence was the series of mergers and acquisitions, which has now come to characterise this period of innovative activity. Walsh & Lodorfos (2002) distinguish four primary types of M&A activity.

1) Vertical mergers between firms with business in successive processes in the same industry.

2) Horizontal mergers between firms in the same industry.

3) Conglomerate acquisitions between firms in unrelated businesses

4) Concentric M&A between firms in unfamiliar but related fields into which the respective partners wish to expand.
The latter type characterises most current M&A activity in the genomics related industry sectors. However, it became apparent that synergy at the discovery-level was profitable only when both sectors were interested in the sources of chemical novelty, but not in the “gene” area. (Chataway, Tait & Wield, 2003) Functional genomics could benefit both sectors in their search for novel and commercially viable chemicals, but the commercial opportunities/markets in the agro sector diverged significantly from those in pharmaceuticals. In addition, the regulatory environments and political/public responses to the progress of both sectors have had very different impacts. Consequently, the dominant trend has now been for the two sectors to demerge and diversify their activities. However, mergers and acquisitions (M&A) within the pharmaceutical/health sectors have continued apace. Vertical M&A activities have involved pharmaceutical companies acquiring leading biotechnology companies in order to take advantage of their R&D expertise, particularly in the area of monoclonal antibodies. (e.g. Johnson and Johnson acquiring US biotechnology company Centocor in 1999). Horizontal M&A activities between pharmaceutical companies are also showing no sign of stalling, hence the continued consolidation and concentration of the sector. But the question must be asked as to whether this trend can continue indefinitely, and if consolidation through M&A is sustainable in the long-term. A recent European Commission report argues that although the large pharmaceutical, agricultural and chemical industries were the pioneers of innovation in the 1980s, the rise of biotech SMEs and their innovative work has convinced the “giants” to develop new kinds of strategies, and establish stronger and more diversified networks and partnerships. This trend was mutually beneficial as the SMEs gained access to large research funds, and the MNCs acquired technologies they could not efficiently develop on their own. However, the future is still very much uncertain. Will biotech start-ups eventually seek greater independence and autonomy and begin to compete with the MNCs on a more equal footing, or will the MNCs choose simply to buy out any outsiders, and come to regard the dynamics of the start-ups as merely an efficient, yet temporary, conduit for the creation of innovative knowledge and technology? A few of the early biotech companies are now beginning to look more like the pharmaceutical MNCs. Amgen is a prime example of this. It is now one of the world’s largest biotechnology firms, and unlike many others it actually has products on the market and has been in profit for almost a decade. Like many biotechs, Amgen trades at price/earnings multiples twice that of the average big pharma company. (Financial Times, 2001) However, according to Kevin Sharer, Amgen’s chief executive, the company has no desire to transform into a pharmaceutical group; rather it will still focus primarily on large molecule therapies. This has traditionally been the main divider between the two sectors, with biotech concentrating on developing proteins in its quest to discover new drugs, rather than traditional chemistry. Large pharmaceutical firms have, on the other hand, focused on small molecules in pill form through the random testing of compounds. Because their fortunes are already built, big pharma now rarely promises percentage earnings growth beyond the mid teens even with one important new product. However, for biotechs hoping to deliver their first drug, any earnings would represent enormous growth. But Amgen doesn’t fit this profile. It has three medicines on the market, and although most of these were based on large molecules it has also begun looking at small ones. For now, according to this article, Amgen’s earnings growth projections are larger than those of big pharma largely because any new product is still being added to only a small roster. (Financial Times, 2001)

Coombs & Metcalfe (2002) argue that traditionally the pharmaceutical industry enjoyed considerable “organic” growth as a result of their patient accumulation of technological
capabilities, marketing and production. They endeavoured to avoid reliance on outside expertise. However, the genomics revolution fundamentally changed all this. The industries have had to combine and co-ordinate capabilities within what is now commonly referred to as a “distributed innovation system”. (Coombs & Metcalfe, 2002, 263) This necessitated increasing levels of M&A activity. The authors claim that the capabilities concept is a useful theoretical and empirical tool for comprehending these new commercial relationships. They write:

‘... capabilities depend on team activity in which the knowledge and skills of the individuals is transformed into the synthetic understanding of the organization. Thus the organization, in all its aspects, becomes an operator for creating the collective from the individual. Since these phenomena are often less than transparent to the external observer --- this has given rise to the idea of causal ambiguity. In short, the link between capabilities and competitive performance is not readily decipherable, even perhaps by the management of the firm, to which its operations are partly a black box --- This raises particular difficulties when a firm comes to choose which other imperfectly understood organizations to engage with in co-operative agreements to generate new capabilities, and similarly, these difficulties arise when organizations consider mergers or acquisitions that will require the combination of capabilities.’ (Ibid. 265)

When analysing the changing configurations of industry structure that are emerging as a consequence of advances in genomics/life sciences, it is necessary to factor in this concept of “capabilities”. Industry itself must recognise the importance of these capabilities when considering M&A strategies. The authors write:

‘... the ex ante analysis of the capabilities in two firms preparing to merge would need to assess capabilities for their similarity, for their propensity to jointly create new capabilities and for their vulnerability to damage if subject to change. These judgements would inform a choice between co-ordination and combination, or indeed a sequencing of these two approaches.’ (ibid. 269)

Moreover, such assessments would need to be sensitive to the potential emergence of unforeseeable developments in capabilities that may be unintended consequences of the merger.

Once we conceptualise M&A activity as being a fundamentally “social process” that is more than simply a transfer of ownership of physical assets and market position, being instead a process which brings together, as James (2002) notes, ‘... distinctive combinations of resources, routines, capabilities, organisations and dominant logics that previously defined separate organisational structures’ (James, 2002, 302), then we can observe and understand industry growth, as well as decline, in a much more interesting fashion. One can begin to illuminate those specific factors that will define whether a merger will succeed or fail, and investigate the extent to which actors in the relevant sectors adequately consider social processes in their strategic decision-making. James provides a brief analysis of some of the recent mergers and acquisitions, with this social process factor in mind. Glaxo Wellcome’s 1995 acquisition of Burroughs Wellcome in a hostile takeover was tumultuous, according to James, because the acquisition was
driven primarily by cost savings, and the two companies were institutionally so very different; the former being commercially driven and focused on the “bottom line”, whilst the latter was primarily academic, pursuing research for its own sake. The Pharmacia and Upjohn merger was even tenser, despite complementary research strengths, because of the two companies’ radically divergent organisational cultures. Pharmacia was half Swedish and half Italian, so there was concern that a US location would make it appear as though Pharmacia was being acquired. A neutral location in the UK was eventually agreed upon, but concerns about maintaining good relations among executives from both sides meant that management put off decisions regarding closure of Upjohn’s facilities in the US, and Pharmacia’s in Sweden and Italy. Thus, the “…result of this attempted “merger of equals” was the emergence of separate, often feuding, centres of power with the US, Swedish and Italian sites running autonomous marketing and research operations.’ (James, 2002, 304) A success story, according to James, was the formation of Aventis through a merger of the pharmaceutical and agrochemical businesses of the European companies Hoechst Marion Roussel and Rhone-Poulenc Rorer. The rationale underlying the merger was that it would provide stronger and more productive pipelines for new products. There were challenges, and conflicts of culture, especially since Aventis inherited an ageing and ill-focused product portfolio, low profit performance, and poor R&D operations. Additionally, both merged companies were the product of previous mergers and acquisitions. But the post-merger integration worked out as a result of astute management. Pharmaceutical R&D was integrated and management styles were harmonised. With the continuing M&A activity within and between the relevant sectors, it is important to consider both “happy” and “unhappy” mergers, and investigate the underlying reasons as to why some succeed whilst others fail. This will become increasingly important in the post-genomic era, because the various industry sectors are often forced into these new kinds of organisational patterns. This project will be well placed to monitor overall industry growth and decline, and look in-depth at rational strategic decision-making “on-the-ground”.

This very broad field of innovation and genomics constitutes within it a number of interdependent sectors and actors whose relationships are constantly changing as internal and external opportunities and pressures exact their influence. There are pharmaceutical/agrochemical MNCs and SMEs, various biotechnology firms with different kinds of expertise to contribute, publicly and privately funded research institutes and university science departments etc. Within individual sectors there are various actors with different motivations, expertise and beliefs in the future trajectory of the technology. (scientists working in ever differentiated fields of enquiry, senior managers, knowledge managers, representatives of trade organisations and regulatory bodies etc) This project will provide not only a general overview and understanding of the various knowledge trajectories and sectoral restructuring that takes place over the next few years, but also offer qualitative analysis on the ways in which actors within the various sectors develop specific strategies to further their interests in response to both foreseeable and unforeseeable internal and external pressures.

**Some Preliminary Research Questions/Issues**

How are the agro-biotech and pharmaceutical sectors evolving as a consequence of the increasing influence of a life science approach to R&D is having on their traditional modes of operation? How do we make intelligent and pragmatic distinctions between the
relevant sectors, the highly differentiated scientific knowledge bases that they are increasingly having to draw upon (chemical knowledge, biological knowledge, molecular biology, bioinformatics and IT in genomics), and the heterogeneous actors constituted within these various knowledge domains? The concept of heterogeneity is fundamental here, and encompasses not only the various actors producing innovations, but also the “users” (healthcare systems, food systems etc). As Gambardella et al (2000) argue, the pharmaceutical industry today must be understood as a system or network in which innovative activities depend on and involve many actors (different types of firms, research organisations, financial institutions, regulatory authorities, governments, health care systems, consumers and physicians.) One cannot look at industry competitiveness by looking only at individual firms, but must observe their dynamic interactions. Dory (2002) countenances this view when he argues that innovation is a process and that the concept of “innovation systems” (local, regional, sectoral or national) provides the best approach to mapping and explaining interactions between the agents who generate and use the technologies. This is a far broader and pragmatic concept to use than inter-industry technology flows in that it:

1) Includes flows that are not necessarily inter-sectoral, such as knowledge flows that occur within firms belonging to the same industry.

2) Takes account of the transfer of both tacit and codified knowledge.

3) It considers flows which occur between different types of organisations and institutions. (Dory, 2002, p. 22)

Economists have provided invaluable data on the macro processes shaping industry growth, and modelled consolidation and competition within and between the pertinent sectors. Pammolli & Riccaboni (2000) offered an empirical analysis of the Pharmaceutical R&D process, and made crucial distinctions between pharmaceutical MNCs who enter the network as drug developers purchasing technologies and licensing-in products, biotech firms that sell molecules through licensing agreements with the developers, and generalist companies offering general purpose technologies. The latter group, the authors argue, occupy a very different structural position within the technology market and enjoy very different risk profiles. (Pammolli & Riccaboni, 2000) The authors also analysed collaborative agreements, claiming that the number of licensing agreements a firm signs can be used as a proxy for its ability to generate knowledge. They discovered that success with licensed-in projects were higher than those of in-house projects, because licensed-in products have a tendency to move through the transition phases more quickly. Another interesting discovery was that US firms have a higher probability of success for in-house products than European companies because they have a higher propensity to subscribe to licensing agreements in the pre-clinical stage. Malerba & Orsenigo (2002) have provided a “history-friendly” model of the long term dynamics of market structure and innovation in the pharmaceutical industry, and found that concentration is shaped by a lack of cumulativeness in innovative activities and market fragmentation. The fundamental importance of the patent is factored into their analysis. Bottazzi et al (2001) have also looked at the growth of the world’s top 150 pharmaceutical firms, using an original database allowing disaggregate analysis at the level of single therapeutic classes and chemical entities. The authors argue that pharmaceuticals is an archetypal “science
Based industry in which innovation of new therapeutic entities and imitation/improvement of existing ones is the primary source of competitiveness, and shapes the dynamics of industry growth. (Bottazzi et al, 2001, p 1162) Within the industry as a whole the authors have observed the co-existence of two types of firms with distinct competencies and competitive strategies. There is an “oligopolistic core” of companies undertaking pioneering R&D who often enjoy first-mover advantages and charge premium prices. Then there are imitative R&D enterprises that generate incremental innovations and competitively priced drugs by taking up licenses from the core and then remaining in the generic markets after patents expire. (Ibid. p. 1163)

These kinds of studies provide useful quantitative data on the processes shaping the evolution of the industry. However, there is a need to buttress such work with qualitative data that looks at these processes “on the ground”, from the perspectives of the actors actually involved in strategic and scientific decision-making. Some of the assumptions made by economists on the status of the sectors may come under scrutiny once qualitative work has been completed. One criticism that can be made of economists’ contribution to this area, particularly evolutionary economists, is that they appear to be only interested in general industry growth, and neglect the possibility of decline. An evolutionary perspective may recognize the fact that individual organizations often go into decline, but they generally regard the overall industry as progressive. A qualitative approach would not make such an assumption, and would look at where the industry is heading not through uncritical analysis of raw de-situated data, but through an investigation of what the relevant actors are doing and saying “on the ground”. Perspectives on what impact genomics technologies have already had on relevant industries, and what influence they are likely to have in the future, are highly differentiated. There are a number of contradictory narratives. Economists often express a rhetoric of growth and maturity, but others are often less optimistic. While some believe innovation leads unproblematically to lots of new and groundbreaking products, others believe that in reality innovative activities rarely live up to their promise. In pharmaceuticals there is little evidence as yet to suggest that the genomics revolution is bringing new and better drugs to market. It may well be changing industry relationships and processes, but it has not yet impacted significantly on associated value chains. The reality and the hype is still very much blurred, and different people have various conceptions of where the industries are heading. Part of this project will investigate these different narratives of change in the pharmaceutical and agro-biotech industries.

The qualitative part of the research will look at the general trends in the sectors from the perspective of the actors involved in shaping the technology and the evolution of the relevant industries. Some of the most pertinent questions are:

1) Where do actors in the relevant sectors perceive the technology to be heading, and how do they develop specific strategies in order that their sector takes full advantage of the opportunities. One would expect to observe significant differences of opinion between managers in SMEs and MNCs, representatives of trade organisations, scientists and managers involved in public sector research, and members of regulatory authorities.

2) How do the relevant sectors view the nature and efficacy of the collaborative process, as well as the increasing M&A activity? How do they see this evolving?
It may well be that the relevant actors are not fully attuned to the long-term projections. In an area where the changes are complex and often rapid, it may be the case that members of the relevant sectors have primarily short-term goals, especially the smaller biotech companies who do not have the financial muscle to think long-term, and proactively seek to shape the innovation process and the evermore capricious regulatory environment. But even the MNCs may also be focusing on the short-term. Some of the mergers and acquisitions seem to suggest that companies are seeking short-term gains at a time when product pipelines are slow. Sidney Taurel, quoted in a Financial Times Life Sciences Survey, argued that “The short term benefits of a merger – which are rationalisations – can boost short term earnings. Yet those gains may only be transient.” (Financial Times Survey, March 15, 1999) But can this trend continue? What is the critical mass of these large pharmaceutical companies? Will deconsolidation be the future trend? Currently the largest firms can absorb the costs of research, but as smaller companies beneath them merge calculations about optimal size could change. (Ibid.) Industry analysts are divided on this issue, so we can expect industry representatives to be equally uncertain of what the future holds.

3) How do members of the relevant sectors view the changing structure of working relationships as M&A activity continues apace, and scientists from various disciplinary backgrounds are forced to collaborate, often in a commercial environment alien to their traditional modes of operation. What is the role of knowledge managers in all this? The success of a merger/collaborative project is often dependent upon the cultural setting; that is on the ways in which previously disparate groups work and integrate with each other in new environments. How the various actors cope with this trend needs further analysis, as it is likely to affect the innovative capacity of the industry as a whole. Richard Findlay, vice president at A.T. Kearney says, in relation to mergers, “A common failure is for companies to look at the physical assets of a merger, the real estate and the products, and to pay too little attention to the intangible assets, the all-important intellectual capital which lies in the people.’ (quoted in Marsh, 1999, p. 111) This view is supported by James (2002)

4) What are the various strategies for innovation in the relevant sectors and how are they impacting on science and industry growth? Here it is necessary to look at issues such as Intellectual property rights, M&A activity, changing structure of R&D processes, knowledge management, collaborative activities and regulatory regimes. These issues must be explored in an international context. The dynamics of the industry in Europe is very different from that in the United States, and the many reasons for this need to be explored in greater depth. Drug pipelines are empty for the foreseeable future, in both the United States and Europe, and big pharma is facing a number of challenges. Reiss (1998) argues that on the economic side healthcare reforms and cost containment measures in Europe and the US are pushing down prices. This is compounded by the fact that fewer new products are being developed. At the same time, cost of development is rising (higher transactional costs as research becomes internationalised, increasing safety requirements, and need for more varied methodological approaches as focus becomes centred on complex diseases with multiple causes.) These problems require that big pharmaceutical firms
collaborate with or acquire small biotech companies in order to sustain drug innovation. Drews & Ryser (1996) argue that big pharma does not itself offer the best environment conducive to originality, lateral thinking, and high productivity, hence the need to outsource research and collaborate. They claim large R&D departments must be fragmented and a broader basis of innovation that is cost-effective must be sought through collaboration. If, however, a small biotech company is particularly innovative and has a potentially profitable product it may begin to look commercially attractive to MNCs, and subsequently runs the risk of being bought out. Some of the scientific research being conducted within small biotechs or publicly funded research institutes may also pose a threat to the very viability of the commercial sector. A recent article in *Chemistry and Industry* reported that researchers have discovered how to convert liver cells of mice into pancreatic cells using a single injection. This may eventually lead to a cure for diabetes. The question is how does the pharmaceutical industry respond to this kind of work? They are interested primarily in treatments not cures. Are they proactively seeking to stall this kind of research? While big pharma clearly needs the expertise of small biotechnology firms, as large bureaucratic R&D departments are unsustainable within the now dynamic and competitive environment of genomics based research (Jones, 2000), not all of these new organisational entities are going to serve the interests of big pharma.

When considering M&A activities it is important to recognise that big pharma companies are not only seeking to buy knowledge but also the "route to market". An increasing trend in the United States is for large pharmaceutical companies to buy Pharmacy Benefit Management companies (PBMs). RAFI COMMUNIQUE (1997) report that Merck, Eli Lilly and SmithKlineBeecham have spent $12.9 billion to purchase the three largest PBMs in the US. PBMs are firms that manage the prescription drugs for health insurance plans. They have preferred lists of drugs for insurance company patients and thus exist as important middlemen between drug companies and their consumers. From the early 1990s the pharmaceutical industry discovered how to control the middlemen, but if controlling them proved too difficult they reasoned that it would be better to simply buy them out. The consequence has been that the range of drugs Americans can get their insurance companies to pay for is narrowing. Ever increasing vertical alliances between the drug industry and healthcare firms are now being established. Drug companies are also crafting deals in which they simply pay PBMs to promote their products. Johnson & Johnson and Novartis have contracts with Value Rx while BristolMyers Squibb and Pfizer have similar agreements with Caremark. (RAFI COMMUNIQUE, 1997) This is indicative of the fact that big pharma will employ a variety of strategies, and realign their M&A activities, in a number of new and differentiated ways in order to maintain their competitiveness. In the agro-biotech field an analogous strategy of "buying the route to market" was employed when the big agro-chemical companies began to buy seed companies.

We need to look more closely at these complex and varied relationships. Who are big pharma merging with or acquiring, what scientific fields are they getting involved in, and where are the convergences and divergences? What will the future be for the SME in biotech? Is it conceivable that some of the smaller firms, especially those focusing on diagnostic tools, could become larger and more profitable than big pharma? Currently, SMEs generally have to work to the strategies of the MNCs because they do not have the financial resources to overcome the evermore cumbersome regulatory hurdles, and
they need the MNCs to commercialise their technologies. Bijman & Tait (2002) argue that the implications this has for innovation is 1) support for SMEs and university spin-offs in biotech is de facto supporting the development costs of MNCs and 2) the need for SMEs to look attractive to big companies constrains their innovation strategies by restricting them to products compatible with MNC strategies rather than potentially competing with them. But can we assume this will always be the case? There is evidence to suggest that currently biotech companies are beginning to slim down. There has been a series of layoffs across the whole sector as a sluggish economy and an increasingly strict regulatory process, as well as lack of investor confidence, has taken hold. (Nature Biotechnology, 2002) Firms are having to refocus on their core research programmes that aim to get products to market fastest.

Another issue concerns publicly funded research. Can we assume that this research will continue to remain in the public sector? University science departments and public sector research institutes are now recognising the need to take onboard commercial values, by spinning-out, spinning-off or spinning-in to a number of new organisational structures. Many have recognised the many benefits that collaboration with big pharma may bring to their life sciences research. But one must ask who essentially wins from these arrangements, and do the collaborations run smoothly? Are MNCs just looking to hijack research at the latter stages in order to reap all the commercial benefits? If this is how it comes to be perceived by the public and regulatory authorities, how will this impact on commercial innovation? How does the industry look at these issues and pre-configure the commercial benefits in an area where nothing remains static and even small changes within or between sectors can, on a cumulative level, reconfigure the entire field? How does their interpretation differ from those involved in SMEs or research groups that remain publicly funded? Are research groups within universities, for example, simply entering into a Faustian bargain when they begin to collaborate with the commercial sector. Many scientists in universities are optimistic that such collaboration will speed up the research process and lead to new treatments for patients being available far sooner. Is this optimism naïve, and what factors will determine the precise benefits reaped by the relevant sectors?

How are these issues different when we compare the pharmaceutical industry with agro- biotech? There is an opportunity here to explore the ways in which very different regulatory regimes and public pressures impinge on industry strategy. It was often assumed that the pharmaceutical industry would not suffer the same level of public opprobrium as the agro-biotech sector, primarily because the pharmaceutical products based on genomics technologies were considered to be far more publicly acceptable on the grounds that they could demonstrate a palpable benefit to the publics' health. However, as genomics research advances, and there becomes a greater movement towards utilising genetic databases, public concern may grow and the industry as a whole may have to develop strategies to placate growing public and political pressure. In the next five years the social, commercial and political environment will almost certainly undergo profound change, and this project will be ideally placed to monitor and understand these developments as they occur.

A More Indepth Look at Some of the Substantive Qualitative Issues
Market and Social Values in the Biotech/Pharmaceutical Sector: A Conflictual or Symbiotic Relationship?

As a consequence of the increasing tendency of biotech/pharmaceutical companies to emphatically embrace globalising strategies (particularly in terms of marketing, manufacturing, collaborating etc) it would be interesting to explore in some detail the underlying motivations and their social and commercial consequences. When industries globalise many groups, particularly NGOs and members of the public sceptical of big business and its unrelenting exploitation of technology, like to define the motivations as purely economic/commercial, which has become a pejorative term of abuse, more so in Europe than in the United States. They often draw the spurious conclusion that market values are here in direct conflict with wider social values, and therefore ought to be heavily regulated. This view fails to recognise that often market and social values are often engaged in a mutually advantageous relationship. In an introduction to the Ernst & Young report, Beyond Borders: The Global Biotechnology Report 2002, Henri A Termeer, President and CEO of Genzyme, dedicated a great deal of rhetorical space to advancing arguments about the global benefits his company will bring to many developing countries. He talked at length of the need for more streamlined and uniform regulatory processes on a global level in order to facilitate genomics-related innovation, economise on the use of resources and eliminate unnecessary delay in the global development and availability of new drug products. This of course can be read as being primarily motivated by commercial exigencies. These developments would certainly serve to augment the profit margins of biotech and pharmaceutical companies willing to embrace a global strategy. But Termeer also talks of the industries' social responsibility, which means acting on behalf of patients all over the world so that they, and wider society, can fully benefit from the biotech revolution. Indeed, Genzyme itself has collaborated with the international humanitarian organisation Project Hope and formed the Gaucher Initiative to provide the drug Cerezyme free of charge to patients in developing regions.

There are two interweaving narratives being deployed here. One is a story expressing the urgency of implementing a uniform regulatory framework that inspires commercial vibrancy and sustainability in a globally evolving biotech/pharmaceutical sector, and the other is an altruistic story on the need to treat the medically afflicted in both the developed and developing world. It is important to understand the relationship between these two alternate values, and the underlying reasons why both are, in particular contexts, deployed by industry representatives. The industry certainly has a lot to gain by expressing a rhetoric of altruism and earmarking resources specifically to aid those in developing countries. On the one hand, it allows individual companies to create a positive public image and therefore possibly forestall growing hostility from interest groups and sceptical Western governments. On the other hand, it allows them initial access to untapped markets which, while not yet able to deliver economic returns, will most likely in the future deal with those companies they are familiar with and have had positive experiences of. So while sceptics may baulk at the industry’s platitudes regarding social responsibility, and look askance when CEOs talk at length of the socially ameliorating benefits of their products, they ought not assume that market and social values are always conceptually distinct and isolated from one another. Even the most commercially motivated actions can bring great social benefits, so industry strategies aimed at creating and sustaining a vibrant global market may not be to the exclusive advantage of the commercial sector. Indeed, hindering the evolution of the
industry by over-regulating it may have hitherto hidden, but potentially serious and extensive, social costs. Interviews may be used to explore further this rhetoric of altruism as a specific industry strategy aimed at creating an environment conductive to scientific innovation.

Questions:

1) Are the social benefits of a vibrant pharmaceutical sector a by-product of economically rational decision-making within companies or a fundamental facet of this commercial process? Reducing the time taken between developing novel drugs and marketing them (a goal that genomics related industries are striving to achieve) is economically attractive, but also satisfies a wider social need for patients to acquire drugs more cheaply and quickly. What is the precise relationship between these two benefits and how do industry representatives both perceive and use them strategically?

2) How far into the future are representatives of the biotech/pharmaceutical sectors looking in developing strategies to sustain innovation? Are the costs incurred by temporary acts of altruistic behaviour seen as a commercially sound strategy for ensuring future returns?

3) How many other companies are involved in similar collaborations to that of Genzyme and Project Hope? Is this an increasing trend?

4) Globalisation: Is this issue different for agro-biotech as opposed to pharmaceuticals? The distinction between the two is not so clear cut. The local may encompass control of the knowledge base, a rather finite concern. But discoveries in biological sciences have global reach and implications. Do local concerns override global ones?

5) How do firms construct markets in their minds and think proactively about directing the regulators? The market/social values distinction is important here. The PITA study discovered that industries in the agricultural sector talked of issues such as sustainability in terms of the “triple bottom line”. This concept recognises the need for financial, social and environmental sustainability, but the industry is keen to stress that without financial sustainability a company will go out of business, and subsequently the social and environmental aspects become irrelevant. How might this concept be useful in considering the strategies of the pharmaceutical industry? Will those companies who advance the need for social responsibility to play a part in the applications of the technology fail to compete commercially? Is there a significant difference in approach if we compare European and US companies? The latter is generally far more driven by commercial necessities.

Knowledge Management

The primary impetus for the increasing trend towards M&A activity in the pharmaceutical industry was the urgent need for high productivity, as measured by new drug output. The realisation that new drug discovery technologies (genomics, combinatorial chemistry and bioinformatics) might reduce the currently long time gap between discovery and marketing of new drugs, as well as render those drugs more effective, motivated pharmaceutical companies to explore and acquire new knowledge bases. Pharmaceutical companies spend vast sums of money on R&D to discover New
Chemical Entities. (NCEs) According to Jurgen Drews, chairman of International Biomedicine Management Partners, such companies strive to discover one new drug per year, but in reality the average is usually closer to 0.4 - 0.8. (Signals Magazine, 1999) He refers to the “innovation gap”, claiming that the number of NCEs introduced by the top pharmaceutical companies cannot sustain the type of industry growth desired. He goes on to claim that the pace of M&A has not yet impacted significantly on productivity, or had any palpable influence on reducing the time taken for drugs to reach market. However, the new genomics/life science related technologies (which constitute a number of different scientific disciplines) will almost certainly have an effect on the pace of drug discovery in the future. However, all this is contingent on the ability of the relevant sectors to sustain innovation and manage effectively the increasingly complex knowledge bases that are being integrated through M&A activity and collaborative networks. A number of questions arise when we begin to consider innovative knowledge management and collaborative/M&A activity.

- How is “knowledge”conceptualised and treated by different actors and sectors? Knowledge managers are becoming ubiquitous within both commercial and public sector organisations. Many people assume that knowledge management is pro-knowledge, in the sense that the primary goal and orientation is towards creating more and more knowledge. But there is an argument, which applies particularly to industries such as pharmaceuticals, that what Knowledge Management is really about is exploiting knowledge as cheaply as possible. Sometimes this may require doing “in-house” research or alternatively contracting it out to SMEs, but often the research has already been done in universities or public research institutes, so the industry has only to tap into this freely available knowledge. The City University of London now runs an MSc course in Pharmaceutical Information Management designed specifically for non-scientists working in the pharmaceutical industry. The aim of the course is to train these individuals to mine the scientific knowledge base for commercially useful information. These people therefore operate with a very different conception of knowledge than academics. One would expect academic scientists to still be attached to the Enlightenment idea of knowledge as a good in itself; that is the more knowledge the better as this is the primary driver of progress. But to the new breed of knowledge managers, knowledge is reconceptualised as a “necessary evil”; the more knowledge there is the more difficult it is to manage and use. So what Chief Knowledge Officers in industries such as pharmaceuticals desire is useful knowledge that is relatively simple to organise, manage and apply. Students taking such courses as that offered by City University are trained to mine the literature and separate the useful from the useless. Individual firms cannot afford to explore every conceivable research opportunity, hence the need to outsource research and increase M&A activities. This knowledge management aspect is an additional, and relatively cheap, strategy to cut back on expensive R&D, and requires deeper analysis precisely because it fundamentally re-configures the nature of traditional knowledge systems.

- Again, there is a need to understand more fully the nature of the various scientific knowledge systems being tapped into by the relevant sectors, and the ways in which the different actors cope with having to fundamentally re-configure their traditional mode of operation when collaborating with scientists, managers,
funders etc. in new kinds of working environments. To what extent do senior managers, and Chief Knowledge Officers, in the relevant sectors rationalise and manage effectively these relationships in ways to maximise the quantity and quality of innovation?

Regulation and Innovation

The nature of the regulatory framework within which the relevant sectors must operate is fundamental to the innovative process, and an issue that industry must be intimately concerned with. Regulatory regimes are multifaceted and here I will mention a few that directly shape industry strategy, particularly in the field of pharmaceuticals.

Government policy

Governments around the world are eager to promote a productive and profitable commercial sector, and therefore are continually having to balance policies that promote innovation with public concerns, both reasonable and unreasonable, about the unrelenting growth of commercial organisations and their impact on prevailing social values. As a consequence of the growth in genomics/biotechnology research, the UK government has been keen to support collaborative R&D. One only has to look at the Department of Trade and Industry’s 2001 science and innovation strategy to see how much interest there is within government to supporting the pioneering work of SMEs through regional innovation strategies. LINK, managed by the Office of Science and Technology, is the principal mechanism in the UK for supporting collaborative R&D between UK industry and the science base. Across Europe, governments are striving to promote industry competitiveness and improve the quality of publicly funded research. They have recognised that it is not enough simply to encourage investment in R&D, but that inefficiencies need to be addressed in other parts of the innovation system, which are often the result of inflexible institutions, communication gaps, lack of finance and networks, and paucity of mobile skilled labour. (DTI, 2001, Annex E)

In the commercial life sciences, Europe lags significantly behind the US in terms of competitiveness and innovation. A number of reasons are often given for this, such as that the US has a more dynamic and interactive business culture that is conducive to networking and collaboration (Financial Times, 2002, p 17), the US government has for far longer encouraged synergy between public and commercial research sectors, and that the US is not characterised by the same degree of division of labour as Europe. Allansdottir et al (2002) argue that another reason for US dominance lies in the strength of its Dedicated Biotechnology Firms (DBFs), which are small specialised firms whose explicit aim is to exploit life science technologies for various industrial purposes. There are a variety of reasons for the different organisational structures and levels of industry growth between the two continents, and within Europe itself, which need to be looked at in relation to how they affect specific industry strategies in the relevant sectors. Many governments in Europe, and industry representatives, have intimated their desire to imitate the US model. It is therefore necessary to explore the effects this may have on the future trajectories of the science and industry knowledge base.
The lack of global harmonisation with many of the policies for promoting innovation is also affecting the relevant sectors and their innovative strategies. The lack of global uniformity on the criteria for conducting clinical trials is one area where pharmaceutical companies have been enabled to expand into other countries to perform life science research. The fact that genomics-related research often requires the testing of “unique” ethnic groups has often been the primary impetus for this particular strategy. This of course raises a myriad of problems, both ethical and managerial, but also new opportunities. (Ernst & Young, 2003, pp. 2/3) But for now I want to concentrate briefly on patents, as policymaking in this area is fundamental to the promotion of innovation in pharmaceuticals, particularly in the post-genomics era.

**Intellectual Property Rights**

As Howells (2002) argues, ‘… in order to protect large research and development expenditures, the pharmaceutical industry relies heavily on intellectual property rights. However, pharmaceutical companies face continuing pressures arising from increased R&D costs and the depreciating value of patents, as patent life is eroded by testing procedures, and pressures have come from public authorities striving to cut health care costs.’ (Howells, 2002, 356) The trend towards M&A activity, concentration of products less affected by government reforms, and orientation towards innovative and high selling drugs represent just some of the strategies industry is employing. (Ibid. p 356)

With regard to patents, which more so in the pharmaceutical sector than any other are fundamental to innovation, the industry has often had to be proactive in furthering their interests through the promotion of strong patent protection. The influence patenting legislation and procedures has had on shaping pharmaceutical industry growth cannot be understated. Archibugi (1992) recognises their importance when he promotes their use as an indicator of industry evolution. He cites as particular advantages:

1) Patents represent in tangible form the outcome of the inventive process, capturing the proprietary and competitive dimension of technological change.

2) Because patent protection is time consuming and expensive applications are likely to be for innovations most likely to provide benefits that compensate for the costs. (large corporations are therefore in a better position to use patents as a strategy of protecting their innovative activities)

3) Patents are broken down by technical fields, and therefore provide useful information on the rate and direction of inventive activity.

4) Patents statistics are available in large numbers. (Archibugi, 1992, 358)

However, he does note some disadvantages also:

5) Not all inventions are patented. Industrial secrecy is often used as an alternative protection strategy.

6) Firms have a different propensity to patent in each national market, depending on their commercial expectations. National market size and level of integration in international trade affects the number of foreign patent applications received by each country.
7) Despite international patent agreements, national patent offices have their own institutional characteristics. (There is growing pressure in Europe to streamline this process in order to aid innovation. The 1998 EU Directive was aimed at streamlined legal protection of biotechnological innovation. The goal is eventually to establish a Community Patent in order to kick-start European competitiveness. See Ernst & Young, 2002)

Patents are a controversial issue, especially in the field of genomics. The Nuffield Institute has recently criticised the idea of DNA patents, claiming they should exist as the exception rather than the rule. The criteria that patents be novel, inventive and useful have not been applied stringently with regard to DNA sequencing. (Reported in Nature Biotechnology, 2002)

However, there are two sides to the patenting issue. On the one hand patent protection provides incentives for companies to take risks and spend vast sums of money on R&D. Grabowski (2002) refers to a number of studies by economists which have shown that managers in pharmaceutical firms regard patenting as the most important and necessary factor in appropriating the benefits from innovation. This, it is argued, ensures that the social benefits of innovative activity are enjoyed by all. However, using patents strategically, it is argued by some, can actually stifle innovation. Recently, the US senate has moved to reduce the time it takes to introduce generic competition against brand-name drugs. Traditionally, pharmaceutical companies file lawsuits when their patents are challenged and are granted a 30 month stay during which time rivals cannot enter the market. But many companies began exploiting the rule by filing multiple lawsuits and receiving multiple 30 month stays. The proposed law would limit companies to one single stay per drug.

Pharmaceutical companies will use a variety of strategies to ensure they reap the full rewards offered by patented technology. Much of the M&A activity is itself the consequence of large companies wanting to get their hands on patents owned by SMEs. The increasing numbers of public research institutes and small biotech firms playing the patent game is a relatively recent phenomenon, one that did for a while trouble the larger pharmaceutical companies, as it threatened their ability to form cartels. Drahos and Braithwaite (2002) write ‘The Pharmaceutical Manufacturers Association in 1992 sounded a cautionary note on the patenting of gene sequences, arguing that government ownership of gene sequences was undesirable.’ (Drahos and Braithwaite, 2002, p. 156) Undesirable mainly for the commercial sector who did not wish to see commercially profitable information in public hands. Drahos & Braithwaite describe many of the negative aspects of the patent system through an analysis of the ways MNCs sought to shape policy in order to protect their interests and stifle competition. Pfizer was particularly concerned with the lack of patent protection in many developing countries and was pro-active in trying to get globalised intellectual property rights established. One of their strategies was to link intellectual property rights and investment with the trade regime, and by sitting on committees and networking with relevant government agencies they tried to turn their desire into reality. Another more surreptitious strategy has been for companies to apply for patents on chemical inventions that are the same as inventions on which existing patents have expired. The complexity of chemical/genomic technologies combined with the complexity of patent law has allowed such double patenting to take place, with overworked patent offices often missing the deception.
Drahos and Braithwaite cite Eli Lilly as one company that has used this strategy in the past.

Companies’ increasing desire to forge links with universities may be partly influenced by the patenting issue. Many MNCS are often dependent on public science in the fields of biotechnology and genomics. Drahos and Braithwaite point to the statistic that 70% of scientific papers cited in biotechnology patents originated in public science institutions, compared with 16.5% that originated in the private sector. The US private sector needs funding of basic research to continue, but the challenge is to find ways to uplift this basic research from the public sector into the private. The authors write, ‘Patents, instead of being a reward for inventors who place private information into the public domain, have become a means of recycling public information as private monopolies.’ (Ibid, p. 165)

Heller & Eisenberg (1998) also argue that the increased privatisation of biomedical research, justified as a means of avoiding the “tragedy of the commons”, may paradoxically stifle innovation. They write: ‘A proliferation of intellectual property rights upstream may be stifling life-saving innovation further downstream in the course of research and product development.’ (Heller & Eisenberg, 1998, 698) The authors refer to this as the “tragedy of the anticommons”, where resources are underused because ‘… multiple owners each have a right to exclude others from a scarce resource and no one has an effective privilege of use.’ (Ibid, 698) The authors claim that in theory, ‘… in a world of costless transactions, people could always avoid commons or anticommons tragedies by trading their rights … In practice, however, avoiding tragedy requires overcoming transaction costs, strategic behaviors, and cognitive biases of participants, with success more likely within close-knit communities than among hostile strangers.’ (Ibid, 698) Privatisation engenders both promises and risks. Patents may protect upstream discoveries and create incentives for innovation, and thus equitably distribute profits across all stages of R&D. But privatisation can go astray when too many owners enjoy rights in previous discoveries that constitute obstacles to future research. (Ibid, 698) Upstream patent rights are increasingly conceptualised as entitlements by those who undertake publicly funded research. Researchers feel they are entitled to co-inventor on a patent, and whilst researchers and institutions resent the lack of access to the patented discoveries of others, nobody wants to be the last one left dedicating their findings to the public domain. (Ibid, 698,699) The authors write:

‘The problem we identify is distinct from the routine underuse inherent in any well-functioning patent system. By conferring monopolies in discoveries, patents necessarily increase prices and restrict use … The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing of the pace of downstream biomedical innovation.’ (Ibid, 699)

The authors also point out that co-owners of a particular patent may have very different, and indeed conflicting, agendas. For example, a government agency may use intellectual property to ensure availability of new drugs at cheap prices, but a commercial pharmaceutical company may want to use the intellectual property to augment profit margins and satisfy shareholders. The authors cite the co-ownership of the patent rights
to the HIV drug azidothymidane between the NIH and Burroughs-Wellcome, as one striking example of how different kinds of institutions can find themselves in conflict over the dissemination of joint property. They write, ‘When owners have conflicting goals and each can deploy its rights to block the strategies of the others, they may not be able to reach an agreement that leaves enough private value for downstream developers to bring products to the market.’ (Ibid, 699) The authors conclude by stating: ‘An anticommons in biomedical research may be more likely to endure than in other areas of intellectual property because of the high transaction costs of bargaining, heterogeneous interests among owners, and cognitive biases of researchers.’ (Ibid, 701)

By looking at the patent system, and the myriad ways in which the public and private sectors involved in genomics related research use it, may enhance our understanding of the changing industry structures and relationships, and the processes of innovation that shape them. Comparisons between generic drug manufacturers licensed to manufacture drugs and original innovators would be particularly useful here. Lichtenberg & Philipson (2002) have looked at the dual effects of intellectual property regulations, from an economic perspective, by focusing on within and between patent competition in the US pharmaceutical industry. Within patent competition characterises the phenomenon of imitators producing generic drug products after a patent has expired, which destroys innovative returns. This is “uncreative destruction”. Between-patent competition characterises the phenomenon of competitors who develop new patented products. This is “creative destruction”. The authors write: ‘A patent only protects an innovator from others producing the same product, but it does not protect him from others producing better products under new patents.’ (Lichtenberg & Philipson, 2002, 3) The authors argue that the latter may be as important as the former in limiting innovative returns, particularly in high-tech fields. IP regulations therefore have dual effects on both forms of competition. ‘Regulations that may seem effective when only considering their impact on keeping imitation at bay may be highly ineffective when taking into account their impact on between-patent competition.’ (Ibid, 4) The authors raise an interesting issue that ought not be ignored when analysing innovative strategies and the evolution/devolution of the industry sectors.

Having provided a very broad review of some of the substantive issues connected to the topic of innovation processes in genomics industry sectors, I want to conclude by setting out a couple of research foci which may be used to guide the project. I will also briefly note some methodological strategies.

**Research Foci**

**Genomics as Transformational of Industry**

This project would look at the complex dynamics of industrial transformation in pharmaceuticals and agro-biotech. In this paper I have talked at length about the social process of M&A activity, but M&A activity on its own does not capture the complexity of the changing science and industry landscape. Therefore, the focus needs to be broader in order to capture the heterogeneity. This focus will look at the social processes underlying M&A activity within the industry/science sectors, and also the value-chain more generally. It will encompass not only an investigation into the changing
alliances/collaborations between the various actors and constituencies who are innovating, but also the role of “users” in shaping the various science and industry trajectories. Comparative studies will be made between the agrobiotech/food and pharmaceutical/health sectors.

**Conflicting Narratives of industry/science growth and decline**

This focus will describe and explain the different narratives and rhetorical strategies deployed by various actors in their understanding of where the technology, science and industry is heading. As explained earlier, some see the industry/science sectors maturing, whilst others conceptualise big pharma as “shell”. This project will investigate these various narratives, and try to understand what kinds of future trajectories are most likely to materialise.

**Managing Interdisciplinarity in Pharmaceutical and Agro-biotech R&D**

This focus could look more deeply at the changing relationships between scientific actors and disciplines in genomics related research within the various industry sectors. One project could be on the increasing need for Information Technology expertise in pharmaceutical innovation, and the ways in which new kinds of knowledge are appropriated, integrated and managed. How is the status of knowledge reconceptualised once it moves between industry sectors with very different goals?

**Brief Methodology**

- Search the academic literature for existing research on innovation strategies in the relevant industry sectors to see what this project can contribute to and build upon.

- Consult relevant databases to get a clearer idea of who the key players are, what kinds of innovative activity are dominant, where M&A activity is concentrated etc. This may provide useful information to help us map the field and decide on which companies we want to study in greater depth. Company annual reports may also prove invaluable in this regard.

- Questionnaires could be used early in the project to help us narrow the field and clarify the most important issues/questions that will inform the more in-depth qualitative interviews.

- Qualitative interviews will be conducted with representatives of the relevant sectors (managers in SMES and MNCs, trade organisation representatives, scientists in all sectors, knowledge managers etc) The focus here will be on the UK and selected European countries. It may be a good idea to interview a number of different people within the same organisation in order to compare different actor’s perspectives. Case studies could be done on individual companies/organisations.
Initially it may be a good idea to concentrate on the pharmaceutical/health sectors and use the results to inform future research into the agro-biotech/food sectors.

Bibliography


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