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ITEC Working Paper Series
05-13
September 2005

ITEC
Institute for Technology, Enterprise and Competitiveness

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Institute for Technology, Enterprise and Competitiveness, Doshisha University
Working Paper 05-13

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Abstract

This paper investigates the choices made by American, British and German large pharmaceutical companies (LPCs) in their location of internally and externally sourced knowledge for drug discovery research. We draw on extensive interview data to assess the role of in-house laboratories, distributed across different locations, in bringing external knowledge into the firm, and the nature and location of network relationships developed. We find that internal and external networks are much less 'global' than general perceptions of the industry suggest. Furthermore, German firms are somewhat less active in forming external partnerships and their internal research sites are more centrally organised than those of their US or UK counterparts.

Keywords: pharmaceutical industry, MNCs, research function, alliances, location

JEL codes: F23, L15, L24, O3

Acknowledgements

This paper is an output of the project, *The Globalising Behaviour of UK Firms in Comparative Context*, which is funded by the Cambridge-MIT Institute (CMI) and the research project, *Globalization and Vertical Specialization: A four country comparison*, supported by Doshisha University's ITEC 21st Century COE (Centre of Excellence) Program (Synthetic Studies on Technology, Enterprise and Competitiveness Project). We are grateful to Man Wing Timming for her assistance in constructing our database of R&D locations and collaborations.

Locating Knowledge: In-house Research Laboratories and External Networks in US, British and German Pharmaceutical Companies

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I. Introduction

Firms that compete in knowledge-intensive industries are said increasingly to conduct their research in globally dispersed, decentralised laboratories, and complement them with external networks of strategic alliances that are spread around the world (e.g. Edler 2004; Florida 1997; Pearce 1999). This was not the case even a decade ago, when earlier scholars perceived overseas research activity largely in terms of adapting home country innovations to local market conditions, while most R&D was conducted at headquarters. Recent OECD data (2004) indicate that foreign affiliates account for a growing share of R&D expenditure in industrialised countries (ranging in 2000-1 from 15-22 percent in the US, Germany and France, and 30-40 percent in Canada, Spain and the UK). An important aspect of MNC strategy in building innovation networks thus concerns location choices and the coordination between in-house research activity and externally sourced knowledge, yet neither the literature on multinational corporations (MNCs) nor the strategic alliance literature takes both internal and external knowledge generation into account.

Decisions on the location of R&D activity in knowledge-intensive industries are motivated by different considerations than those influencing other functions, such as manufacturing or marketing, where market access may be an issue. The pharmaceutical industry, which is the focus of this paper, is highly selective in its choice of R&D location, with technologically advanced research taking place in relatively few countries and regions of the world (Zeller 2004). Driven by the need to recoup heavy research costs, large pharmaceutical companies (LPCs) seek to market their products across the world and frequently have widely dispersed manufacturing activities, and the industry is thus widely perceived as global. (A ‘global’ location strategy in the literature on MNCs’ additional research centres usually means a presence in each Triad region and, to avoid confusion, that is how we use the term.) But to what extent do even the largest firms conform to this global image with regard to their discovery research activity? Are firms from some countries more ‘global’ in their knowledge sourcing practices than others? Do some firms make more foreign direct investment (FDI) in research sites than others?

The US, UK and Germany have played a leading role in the history of the modern pharmaceutical industry, conducting high levels of research and discovering many of the world's most important drugs. German chemical-pharmaceutical firms ranked among the largest pharmaceutical firms in the world in the 1980s, based on their expertise in organic chemistry but, in the wake of the biotechnology 'revolution', they have been overtaken by US and UK firms (among others) with capabilities in biotechnological sciences.[1] Not only has the basis for much of the work in pharmaceuticals shifted from chemistry to biology, so has the way in which firms organise their resources to discover and exploit knowledge, in order to develop new drugs. Increasing proportions of R&D budgets are spent outside the home country, via FDI and alliances. Scientists in multinational pharmaceutical firms thus draw on three different knowledge bases: the laboratories in which they work; intra-firm knowledge transfers from other (sometimes foreign) R&D facilities; and externally sourced knowledge collected either explicitly through alliances with home and overseas firms and research institutes, or implicitly through knowledge spillovers.

The importance of third parties as suppliers of technology and of drug compounds is evident from the pharmaceutical industry's low R&D productivity over the last 30 years. New drug approvals have since 1970 failed to keep pace with a 50-fold increase in R&D expenditure (Booth and Zemmel 2004). Direct costs have risen due to the complexities of discovery technologies and tougher clinical trial requirements (Buxton and Easton 2003). LPCs have repeatedly reconfigured their research organisations in the 1990s in an attempt to overcome these challenges (Zeller 2004). Technological change has created a division of 'knowledge labour' (McKelvey and Orsenigo 2001 p.16) between the research or technology activity of biotech firms occupying specialist niches on the one hand, and on the other the MNCs that possess the capital and the infrastructure to bring drug candidates through costly development to market. Small biotechnology firms are integral to the reinvention process, but it is the large pharmaceutical MNCs that, by reconfiguring their discovery function, control the overall scope and direction of the innovation process.

In this paper we explore the locational choices made by LPCs headquartered in the UK, Germany and the US with regard to their discovery research capabilities. (We attempt to distinguish between basic research on the one hand, and clinical development work on the other; the latter is probably less crucially tied to specific locations than discovery research, and is not covered in this paper.) We also examine the networks of external research collaborators they construct, and finally we consider the spatial and

relational proximity between LPCs' internal research activity and their external network partners. In each case, we draw cross-national comparisons, highlighting differences in behaviour between US, UK and German firms.

We bring both primary and secondary data to bear on our consideration of pharmaceutical firms' organisation of internal and external knowledge sourcing. In 2003 and 2004 we conducted in-depth interviews with high-level corporate executives within or close to the R&D function in most of the major US, UK and German pharmaceutical companies, as well as in a small sample of biotech firms. (A list of all firms interviewed is provided in Appendix I, which also explains the naming convention we use to disguise their identities). Detailed knowledge of firms obtained from extensive interviews is the only way to identify input-output relationships in and between firms and institutions (Zeller 2001). We additionally constructed a database to capture the locational aspects of external sourcing for the major pharmaceutical companies in each of the three countries, utilising company, industry and analysts' reports. These secondary data provide an overview, in quantitative terms, of the location of external sourcing of knowledge in relation to in-house R&D. Our own more qualitative data are employed to assess the use of external knowledge and the rationale for the locational choices made.

The rest of the paper is structured as follows. Section II discusses first, theoretical perspectives on the internationalisation of MNCs' in-house research functions; and second, the use of strategic alliances in external research network building. We then review the features of the American, British and German systems of innovation pertinent to the pharmaceutical / biotechnology industry and their impact on the ability of firms to respond to technological change. Section III is the empirical core of the paper, in which we explore patterns of knowledge sourcing practices by LPCs from these three countries. In part III.1 we establish the locational choices of in-house research laboratories; how these have changed over time, particularly with regard to the importance of the home base; and how responsibilities are distributed between sites. Part III.2 then examines the geographical aspects of external sourcing practices and the networks thus created. The Conclusion considers the extent to which LPCs' internal and external sourcing networks represent a truly global strategy and whether distinctions can be made between firms of different national origin.

II. Internationalisation of Research: Theoretical Perspectives

Firms are not constrained by national boundaries in their development of knowledge networks. Faust et al (2004 p.21) interpret globalisation as a broadening of the 'space' in which industrial restructuring occurs: firms as strategic actors transcend traditional firm boundaries on the one hand by reconfiguring their value chains to make use of new practices and new knowledge of supplier firms, and on the other by relocating activities. The latter includes the option to move functions abroad or, more frequently, to split the R&D function between various locations, thereby extending firms' strategic scope and, hence, their participation in what Gerybadze and Reger (1999: 255) refer to as a 'polycentric structure of national research and innovation systems'. MNCs traditionally attempted to retain the high value-added discovery function at headquarters, and FDI in research sites has been under-developed as a result. But, because of the highly codified nature of its knowledge base, the pharmaceutical industry lends itself well to a process of disaggregating the value chain across functions and locations. Hence LPCs not only attempt to internalise promising new technologies by monitoring developments on a worldwide basis, via collaborations with research institutes and biotech firms, but also by embedding themselves in specific knowledge-laden regions to achieve "relational and cultural proximity" to key actors (Zeller 2004: 84).

II.1. MNCs and the Internal Research Function

The literature on transnational firms and the globalisation of MNCs' innovation activity charts a shift in more recent times away from a choice of 'classical' strategies between substantially centralised R&D processes or the dispersal of innovation processes to serve local markets. Instead, 'globally linked' approaches permit geographically dispersed units to play key specialist roles in the joint creation and implementation of an innovation (Bartlett and Ghoshal 1989) through the provision of unique resources and capabilities (Pearce and Singh 1992). Dispersed facilities thus hold an inter-dependent position in a firm's core knowledge generation programmes (Pearce 1999). But the literature on the international dispersion of research sites largely assumes that new facilities are established strategically. It ignores the reality that significant M&A activity in recent decades has, as a by-product, extended LPCs' portfolio of research laboratories in a less planned manner, thus rendering their coordination more complex. It further appears to equate internationalisation of R&D with the scattering of innovation activities across the globe, whereas Gerybadze and

Reger (1999) point to a noticeable trend since the mid 1990s towards a strategy of R&D concentration combined with global evaluation of leading-edge locations.

Much of the research on knowledge spillovers focuses on the gains that host countries derive from MNCs' foreign affiliates. Until recently, relatively little work considered the reverse side of the coin: the impact of the transfer of knowledge from host country to MNC. More recent studies have noted that research-related FDI now frequently reflects corporate efforts to harness external scientific capabilities (McKelvey and Orsenigo 2001). This implies a changing relationship between research headquarters and dispersed subsidiary laboratories. Decentralised research facilities are seen to occupy an important position in assuring the strategic competitiveness of the multinational firm (Edler 2004; Florida 1997; Pearce 1999), sometimes displacing an earlier focus on product adaptation for foreign markets. Both strategies continue to exist side by side, and it is too early to say that the new approach has replaced the old. Although the evolutionary model of internationalisation suggests that the primary explanation for decentralisation of R&D is geographical proximity to production sites or other corporate functions, in knowledge-intensive industries different network dynamics are at play (Blanc and Sierra 1999). Technology-oriented motivations have become paramount, such as tapping into the innovation systems of other countries (Cantwell 1998). This is particularly true of the biotechnology sector (Florida 1997), in which technology laggards seek additional knowledge from technology leaders outside their home country. In contrast, MNCs that achieve technological leadership through rapid innovation at home have weaker incentives to internationalise technological acquisition, because of the magnetic attraction of their home-based research (Cantwell 1998). But these firms and their domestic competitors may also decentralise R&D within their home country, to be closer to technology-laden regions.

Pearce (1992) shows that US MNCs are generally less attracted by the distinctive scientific, educational or technological strengths of overseas locations for their R&D functions than are European or Japanese MNCs. Furthermore, security concerns over intellectual property prevent the establishment of important discovery research bases in countries where patent protection is weak (Taggart 1991, Interview Notes 2003-4). Research site dispersion is thus limited mainly to Triad regions. Nevertheless, for many firms, R&D activity remains concentrated at headquarters and is supplemented by new sites charged with developing complementary knowledge or specialising in aspects of early stage discovery work. Research site dispersion, perhaps internationally, should not be confused with decentralisation of control.

Strategic reassessment of decentralised R&D organisations, dispersed across numerous sites often accumulated through merger activity, has led in recent years to the practice of designating one or more laboratories as a 'centre of excellence' (COE). Closure or, more often, rationalisation or refocusing of other sites frequently accompanies such reorganisation. Frost et al (2002, p.997) define a COE as "an organizational unit that embodies a set of capabilities that has been explicitly recognized by the firm as an important source of value creation, with the intention that these capabilities be leveraged by and/or disseminated to other parts of the firm". Whereas Frost et al (2002) suggest that a COE is rarely to be found in a foreign subsidiary, other researchers find that transnational firms from countries that lack the necessary institutional infrastructure in a particular field do indeed so designate specialist foreign research units (Gerybadze and Reger 1999). Firms establish COEs either in a location where substantial relevant in-house scientific resources are already gathered, or where external resources are clustered. In the case of biotechnology, for European and Japanese LPCs this is often (though not always) in the US. Another form of research reorganisation (followed e.g. by GSK) is based on the recognition that discovery research does not respond to economies of scale in the same way that clinical development work does. It therefore attempts to re-create the ambiance of nimble biotech operations by breaking up colossal laboratories into smaller, focused units spread around the global network. As such, each CoE enjoys some autonomy of action, yet the technological trajectory it follows remains coherent with the long term plans of the MNC (Frost, et al. 2002; Pearce 1999).

Reorganisation and rationalisation of research units does not come without human and organisational cost, however. Closure of research facilities is much more problematic than the shuttering of manufacturing sites because of the long-term nature of much scientific work and the relationships created with outside institutions. The strategic management literature tends to gloss over these difficulties, beyond noting the need to effect a smooth transition to the new arrangements. Yet, if an MNC is to achieve efficient intra-firm transfers of knowledge from one COE to another, or from a COE to a development unit, it will require a different set of managerial practices (knowledge management in combination with information and communication technologies) than the traditional top-down mechanisms. Proponents of the centralised system of research, where most activities are conducted at a single site close to corporate headquarters, argue the benefits of close proximity for scientists working on a particular project, in terms of ease of communication and decision-making, compared

with the time, travel and fatigue associated with gathering team members from widely dispersed sites. The tacitness of some information and the need to invest in related information and skills in order to exploit such technological knowledge, highlights the possible 'stickiness' of innovative activity as well as the high costs of achieving complete information transfer between locations (Von Hippel 1999).

Thus far we have considered only direct investment as a means of engaging in dispersed knowledge-sourcing activities. An alternative or, more usually, complementary strategy is for MNCs to form 'scanning units' with the specific role of prospecting for and transferring knowledge to headquarters. Such units may be co-located in important dynamic environments (Frost, et al. 2002), or they may comprise teams or individuals travelling from headquarters to these regions (Interview Notes 2004). The literature on MNCs pays little attention to *how* firms go about the process of accessing external technology, and we therefore turn to the innovation and strategic alliance literatures to consider this strategy in greater detail.

II.2 Network-Building through Strategic Alliances

The need for LPCs to improve their drug pipelines and raise productivity in the face of significant patent expiries and rising development costs is already well documented. For firms with stock market listings in the US and the UK, pressure from shareholders makes this need particularly acute. Even in Germany, where shareholder pressure for improved performance is a relatively recent phenomenon (Becker 2001), calls are being heeded. Firms are increasingly turning to external partnerships to supply compounds for their early, medium and late stage pipelines. The pace of technological change in the life sciences further contributes to the growth of collaborations with specialist technology suppliers. Furthermore, the nature of scientific endeavour in and the rigorous regulatory control over the development of new medicines means that substantive external knowledge sourcing will generally involve partnerships with firms lasting for years.[2] One survey of large pharmaceutical companies found that six in ten firms were spending at least 10 percent of their R&D budget on alliance activity, whereas only one in ten were spending this amount five years earlier (Aitken, et al. 2000). Strategic alliance formation as a competitive strategy has thus become a fact of life in the pharmaceutical industry. Discovery research alliances can be relatively easy to discontinue and are less expensive and more flexible arrangements than direct investments, but agreements are becoming increasingly complex, heterogeneous and idiosyncratic (de Rond 2003). Collaborative arrangements may be fragile not only

because the risk of research failure is high, but also because of shifting priorities by partners, particularly when firms go through mergers. Once formed, alliances exist in a continual state of negotiation and iteration. Successful research alliances may, and often do, evolve into licence agreements. In the later stages of clinical development, however, compound licensing agreements are rather less flexible and require far greater investment.

The networks of external knowledge/technology providers that firms construct may have a strong orientation towards knowledge-laden regions and physical proximity (Castilla, et al. 2000; Storper and Salais 1997), they may be mainly nationally oriented or, in a highly globalised industry, firms may aim for global innovation networks. Relationships between LPCs and the various research environments in which they operate have become more interactive than in earlier times, when research and development value chains were less fragmented across corporate and national borders. Decisions over the geographical focus of scanning for external technology providers become linked to organisational decisions about how to integrate the work of such partners into internal research strategies. It is likely that, if a firm's internal and external research activities are integrated, diffusion of knowledge within the firm will take place more effectively than if the products of the two networks are kept separate.

Scanning the environment for new promising compounds can occur either in a centralised or a decentralised manner, i.e. from a central research site at the headquarters supplemented perhaps by periodic visits to a set of interesting countries, or via investment in additional research facilities located in knowledge-intensive countries and/or regions that are charged with building networks in host countries. MNCs pursue both these strategies, sometimes in combination.

Any shift in organisational emphasis by LPCs from centralised research with dependent subsidiary laboratories to a more distributed, de-centralised organisation has implications for the types of linkage made with the research community around the subsidiary facilities. Affiliations between firms and the scientific community are personal rather than corporate, based on the professional reputation of the individuals involved. Powell et al (2005) point to the importance of firm/institute reputation in the forging of links between various actors in collaborative research networks (Powell, et al. 1996). Yet it is the human capital within a research laboratory that dictates ties to the external environment. Dependent subsidiary facilities will attract relatively few highly qualified personnel, and most staff affiliations will be local, whereas semi-autonomous

CoE sites will house highly qualified scientists with circles of affiliation at local, national, regional and global level (Lehrer and Asakawa 2003). Multi-level connections can be exploited across the firm, unlike the more limited usefulness of local affiliations. This argument may imply that geographic proximity to knowledge-laden regions is less crucial for a CoE than for a dependent research laboratory, but in practice co-location advantages are too strong for most MNCs to ignore. Foreign scientists employed by an MNC naturally associate their own, differently organised, occupational communities, and it is in the interests of the MNC that they foster these relationships, to remain at the cutting edge of their research.

Lehrer and Asakawa (2003), in their study of US and Japanese research laboratories in Europe, identify asymmetric abilities among MNCs to interact with host country technologies and competences, based on different home-country systems of innovation favouring tacit or explicit knowledge flows between firms. Perhaps not surprisingly, the US firms were better able to navigate the European systems using European scientists than were the Japanese firms. The national background of an LPC may thus influence its ability to exploit overseas knowledge bases. As de Rond (2003) argues, alliances are after all social phenomena, whatever the underlying business rationale. To negotiate a deal, let alone operate the alliance successfully afterwards, requires some common understanding of processes and procedures.

II.3 Innovation, Change and Supporting National Institutions

Significant consolidation occurred among stock-market-listed US and UK pharmaceutical firms in the 1990s, driven by the search for economies of scale and global marketing reach, but not among the German sector's family-dominated pharmaceutical firms. (Hoechst was the exception.[3]) Further, the distribution of biotech firms varies internationally and so does the maturity of incumbent firms. Both aspects point to important differences in national institutional arrangements that facilitate or constrain firms in their development of organisational solutions to the problems of declining research productivity. A nation's innovation system influences the type of research conducted and its intensity, reflecting earlier patterns of technological strength and shaping the development of subsequent technological competences (Cantwell and Molero 2003; Nelson 1993). Social acceptability influences the willingness of firms to engage in or invest in biotechnology/genetic engineering research (Reger 2000 p.127). The positive public attitude prevailing in the US and the UK since the 1970s was not mirrored in Germany until the mid 1990s, with detrimental effect on domestic

investment in biotechnology. In contrast to the many US biotech firms that have reached profitability and have one or more products marketed and/or in late stage trials, and a British sector that leads other European countries while still trailing the US, German biotech firms are only in the process of transition from providing technology tools for other actors to developing therapeutic products of their own (Ernst & Young 2003a, 2003b).

Many observers regard the qualitatively different industry-university relations in the US compared with those in Europe as a central factor shaping the differential development of biotechnology competences. Whereas university researchers in the US play key roles as founders, consultants and scientific advisory board members of science-based start-up firms, legal prohibitions in European countries such as Germany have, in the past, prevented faculty involvement in the commercialisation of science (Lehrer and Asakawa 2004; Owen-Smith, et al. 2002). The funding system for universities and public research institutes influences not only the amount of research that gets done – the US National Institutes of Health annual budget of around US$24 billion dwarfs European science funding, and elite institutes additionally possess their own generous endowment funds – but also the possibilities for collaboration between scientists. European scientists are more dependent on 'core' funding than on the competitive grants that are the norm in the US (Hicks 1993), and the centralisation that this entails brings with it both greater hierarchical control and fewer opportunities for multi-disciplinary collaboration (Owen-Smith, et al. 2002). This is particularly the case in Germany, where the elite Max Planck institutes are organised around single research fields (e.g. biochemistry, immunobiology, molecular genetics), compared with the multi-disciplinarity of US top research institutes (ibid.).

Easy labour mobility between university and the private sector, as in the United States, supports a dynamic entrepreneurial environment where high tech start-up firms have the flexibility to develop or abandon research competences by hiring and firing scientists and technicians (Casper and Kettler 2001). The movement of people between firms facilitates the efficient exploitation of research networks and the rapid commercialisation of scientific ideas, creating the potential for radical innovations. In Germany (and to some extent the UK), on the other hand, social stigma is attached to corporate bankruptcy or frequent job changes. As a result, fewer high tech firms emerge, scientists are more reluctant to join ventures where the risk of key project failure is high (as it is in biotechnology), and there is no ready flow of employees with crucial business skills from large stable firms to young high tech enterprises (Casper and Kettler 2001).

Firms' attitudes to technology acquisition influence the collaborative arrangements they are able to make (Hemmert 2004). As 'decisive buyers' of promising research results, LPCs support the creation and growth of start-up firms (Reger 2000 p.130), generating a dynamic market for new technologies in which firms both within and outside national borders can participate. The presence of cutting-edge technology and know-how in US academic research institutions has turned the country into a magnet for biotechnology-related inward investment and raised concerns over the extent to which European research-based pharmaceutical companies are transferring their R&D expenditure to the United States (EFPIA 2002).[4] US LPCs arguably now have little incentive to locate significant R&D overseas, because of the strength of the domestic biotechnology infrastructure (Gerybadze and Reger 1999).

The early emergence of a developed stock market in the US and UK turned M&A into the means by which firms grow, while also releasing surplus managerial capabilities into the labour market. Bank-centred German industrial growth supported the continuation of family-run firms, which had greater incentives to pursue prudent internally funded expansion and strategies for organic growth. These differences in ownership structures fundamentally influence both the mode of firm growth and the degree of pressure on owners to respond to a changing competitive environment (Hall and Soskice 2001). The recent erosion of banks' influence in Germany suggests that the notion of 'patient' capital is no longer the most important institutional arrangement governing firm behaviour, yet the co-determination system continues to impose financial penalties on firms pursuing 'hire and fire' policies and hence still encourages long-term stable employment.[5] In these circumstances key functions such as discovery research are more likely to be home-centred in German firms than in UK firms, which also do not enjoy the market-scale advantages of US firms. Further, strong employment regulation in the German system poses internal barriers to the easy acquisition and shedding of labour and skills seen in the US and the UK.

These distinctive national institutional frameworks encourage or constrain firms' attempts to reorganise their value chain, across the boundaries of the firm and across borders. We turn now to our empirical data to examine their effect on firms' locational strategies.

III. Internal and External Research Networks in US, UK and German firms

Where, then, have US, UK and German LPCs invested in research sites, and what patterns are emerging from any reorganisation of their research networks? Further, where are the sources of their external knowledge located and how do firms use their internal resources to access them? To assess whether a company follows a decentralized strategy of external knowledge sourcing through multiple R&D locations in several countries, we adopt a mixture of input and output measures and supplement them with our own more qualitative interview data on various aspects of locational strategy and associated organisational choices. To gain input measures, we analysed company data on the location of major research sites, gauging their relative importance through employment data. Our output data are derived from an analysis of publicly available information on research collaborations and the geographical origin of successful in-licensed drugs.

III.1 Trends in Internal Research Locations

The supremacy of the US in both academic and commercial biotechnology, described above, is continually reinforced both by growing FDI in discovery research sites and by the migration of scientific talent to the US, particularly from Europe. According to the EFPIA (2005), 70 new molecular entities (NMEs) were invented in the US in the period 2000-2004, compared with only 57 in Europe. In this context, the R&D orientation of US companies may justifiably remain US-centric, with a strong regional orientation towards the biotech-rich West Coast and/or Boston area. The issue for European LPCs has become how to manage their home research sites while also participating in the richness of the US field.

Table 1, drawn up from publicly available resources, indicates the main discovery research locations (excluding minor supporting sites) of leading US, UK and German LPCs in 2004-5. On average, US LPCs firms have 3-4 domestic sites and one overseas research facility, while German and British LPCs' research facilities are more evenly spread between the US and Europe with 1-3 major sites in each region. With regard to US LPCs' domestic locations, our analysis of employment patterns largely reflect the findings of the Milken Institute (2004) that California (especially La Jolla and San Diego), New Jersey, New York and Pennsylvania are the most important for the bio-pharmaceutical industry. The few instances in our sample of US LPCs recently opening (rather than acquiring) new R&D sites have been exclusively in the Boston area.

Table 1: Principal discovery research locations of LPCs and major US biotechs*

	US	Europe	Japan
US firms			
Abbott Labs	IL,MA	D	
BMS	NJ(3),CT	B	
Lilly	CA,NC,IN(4)	UK,D	yes
Johnson & Johnson**	CA,NJ(2),PA(2)	B(2)	
Merck	CA,NJ,PA,MA,WA	I,ESP,UK	yes
Pfizer	CA,MA,MI,CT,MO	UK	yes
Schering-Plough	CA,NJ	I	
Wyeth	NJ, NY,PA,MA		
Amgen	CA,MA,WA		
Biogen-IDEC	CA,MA		
Genentech	CA		
Genzyme	MA(2)	UK	
UK firms			
AstraZeneca	MA, DE	S(2), UK	small unit
GSK	NC, PA(2)	I, UK(2)	yes
German firms			
Altana	MA	D	
Aventis***	NJ, MA	F, D	
Bayer	CA, NC, CT	D	yes
Boehringer Ingelheim	CT	AU, D	small unit
Merck	MA	D	
Schering	CA	D	small unit

CA=California, CT=Connecticut, DE=Delaware, IL=Illinois, IN=Indiana, MA=Massachusetts, MI=Michigan, MO=Missouri, NC=North Carolina, NJ=New Jersey, NY=New York, PA=Pennsylvania, WA=Washington

AU=Austria, B=Belgium, D=Germany, F=France, I=Italy, ESP=Spain, S=Sweden, UK=United Kingdom

* excludes smaller discovery units
** includes autonomous subsidiary sites
*** pre merger with Sanofi Synthélabo (France)

Source: compiled from corporate websites and public databases

But these firms in recent years have not chosen to open new R&D sites in Europe. Conversely, British and German firms have been opening, and actively continue to open, new facilities in the US for the purpose of benefiting from local external knowledge spillovers. Their choice of location for these new subsidiaries/institutes is consistently the Boston area or California, close to leading universities and technology hotspots, rather than in the proximity of their existing pharmaceutical operations clustered in New Jersey and around Philadelphia. At the same time, concurring with the EFPIA data cited

earlier, neither our British nor our German firms have recently opened new research facilities in Europe. Japan, the world's second largest pharmaceutical market, has also failed to attract significant discovery research activity from other Triad LPCs, although several US, German and British firms possess smaller research units there that specialise in particular therapeutic fields (as well as often much larger clinical development facilities).

Although precise employment data are difficult to determine since the categorisation of staff between research and development activities is blurred, the database we have constructed indicates that only three US LPCs locate even 20-25 per cent of their researchers overseas and several employ fewer than 5 per cent of discovery scientists outside the US. Yet both the big British firms not only have very substantial research employment in the US (35-45 per cent of their total researchers) as well as in Italy or Sweden (and other Continental European locations), but also have chosen to base their heads of research outside the UK. In contrast, for all the German firms the most important research site remains their home base, at or close to the corporate headquarters.

For US and UK LPCs, both domestic and foreign research locations increased in number as a result of substantial M&A activity, especially in the 1990s. German firms, with one or two exceptions, have been more cautious in their acquisition strategies and hence tend to have fewer (or, at least, smaller) research facilities to integrate. In addition to the main discovery sites indicated in Table 1, many firms have satellite laboratories scattered through smaller European countries/markets (e.g. Finland, Sweden, Italy, Spain) and North America. Germany, however, is not a research location for either US or UK LPCs; nor has the UK attracted pharmaceutical research investment from German LPCs. Firms have acquired some satellite research sites specifically for their specialist supporting technology (e.g. GER-PH-2, UK-PH-2).

We found several instances where decisions on research locations were not taken strategically, and that one or more locations existed simply by historical accident. 'Well, in my view, and I wish I could say that this was entirely driven by some strategic plan, and maybe it should, but it wasn't actually' (US-PH-7). Certainly this was the case with respect to facilities inherited through mergers. Financial incentives are not seen as significant factors in the location of new research facilities either in Europe or the US. Far more important are the presence of particular pools of knowledge, often clustered around major universities, and the availability of skilled scientific personnel. One firm

pointed out that “If we had difficulty recruiting here [in the UK], then we may have to consider relocating [to the US]” (UK-PH-1). The same company noted that certain disciplines, such as bioinformatics, are “hard to find anywhere other than the west coast of the US”, and so “having the facility on the west coast for us is undoubtedly very helpful, actually in the home of informatics”. And yet, a few German firms (e.g. GER-PH-5, GER-PH-3) were keen to stress that some therapeutic approaches and technological expertise were only to be found in Europe, and cautioned against regarding the US as leading in all areas of biotechnological knowledge.

The organisation of discovery research ranges from highly centralised, with the main research site acting as a conduit for all work passing from one subsidiary unit to another (e.g. GER-PH-4), through to highly decentralised, possibly accompanied by wide geographical dispersion. But decentralisation today does not mean autonomy of action, as it sometimes did in the past. One company used to have four sites around Europe that were “independent autocratic organisations”, where “the regional vice presidents of sales and marketing organisations sat round the table with the heads of the sites and they discussed it and decided what they’d take and what they wouldn’t take”; following its merger with another LPC, that autonomy has now been replaced by a “fully integrated global R&D model” (UK-PH-6A). Another firm recently began moving steadily towards greater cross-border integration, overriding the resistance of one foreign site head to the loss of his autonomy, so that “when we develop a product now, it is always a global product” (GER-PH-5B). Cost, regulatory compliance issues, and the need to harmonise standards and procedures to ensure inter-changeability between sites are the reasons GER-PH-1 cites for its own shift during the last 10-15 years towards global organisation of research. Now, headquarters formulates the firm’s strategy, which is then pushed out to all divisions and subsidiaries, and international steering committees based at HQ are in charge of ensuring integration. A few US LPCs have also made moves towards ‘global’ coordination of their in-house R&D activity, replacing a dichotomy frequently found until the late 1990s between the US and overseas organisation that had tended to encourage a US-centric perspective on research.

Many LPCs now operate discovery research in internationally distributed centres of excellence, each with responsibility for specific therapeutic areas. Allocation of therapeutic areas to different sites depends on a mixture of historical tradition – it “doesn't make sense” to outsource the traditional area of strength (GER-PH-6A) – and on where location-specific expertise lies. Existing research networks may also influence the division of responsibilities: “[therapeutic area X] was located here and then it went

to [the US], whereas we still kept [therapeutic area Y] because we had a big network, genomic network, sponsored by the German government, […] of something like fifteen to twenty collaborators [with] several biotech partners but also smaller biotech companies that are specialised in certain areas, like diagnostics, and then university partners, hospital partners" (GER-PH-10). Another German LPC achieved site specialisation by transferring all biopharmaceutical activity to a US subsidiary it had bought, and receiving in return all of that entity's chemistry-based compounds (GER-PH-5). Closer integration brings with it greater rigour in performance measurement, however, even for smaller biotechnology-related research units: "This site here in [location] used to be a research boutique. People could do what ever they wanted to do on whatever time line. We are not like that any more. We have objectives and time lines. We are now much more consistent with the pharmaceutical industry, it made us far more efficient, much more competitive" (GER-PH-6B) – a response also to this firm's greater adoption of the 'shareholder value' principle. In a much-publicised reorganisation of its research with the aim of recreating the ambiance of flexible entrepreneurship, GSK split its discovery research in 2001 into six Centres of Excellence in Drug Discovery, three of which are located in the US and three in Europe (two in the UK and one in Italy); while a German LPC has established a specialist focus in two therapeutic areas in Europe, two in Japan and one in the US.

M&A-induced proliferation of R&D sites has led to recognition that internal research organisations can suffer from over-complexity. This thought process is particularly prevalent among US and UK firms, as German firms suffer less from this problem. But this insight has not necessarily led to significant action. "I think there is certainly a theoretical case to say we have too many sites and it would be sensible to reduce that number of sites [...] I wouldn't argue that what we've got is how you design it, I don't think anybody would design an R&D organisation the way ours is. It's there because of history. If you could snap your fingers and change it without all the pain that goes with it, we would probably change it" (UK-PH-6A). But the 'pain' of rationalising research sites is much greater than for closing manufacturing facilities, "because the relationship with the community is much more integrated. […] You've got the relationships with the local educational institutions and the universities" (ibid). Advantages of multiple sites include "cultural diversity" (UK-PH-6A) – the benefits of which, this respondent acknowledged, were somewhat dissipated by the complexity of the overall research organisation – and greater productivity "because undoubtedly doing research in Europe is cheaper, if you can do it at the same quality" (ibid.). The caveat

thus expressed was reflected in the avowed intentions of two other firms, both of which planned to close certain sites because "our research investment has had not the productivity it should have" (UK-PH-2A) or because the small acquired site "just wasn't as efficient as I would like" (UK-PH-5). In the latter case the firm planned to transfer the technology in question to its US laboratory, and was also deferring a decision on the fate of a Scandinavian research site until work on a particular technology there had progressed further.

German LPCs, in contrast, appear largely content with their internal network of sites, which in some cases reflects the relatively small size of the firm and limited resources. Reflecting the 'stickiness' of information (Von Hippel 1999), some firms were keen to represent their limited range of locations as a competitive advantage: "we have all research and administration in one location, on this campus, with rather good communication […] And you could even go as far as saying it is like a special spirit – especially in research, I can say that we have a special esprit de corps, everybody knows the aims and goes for it" (GER-PH-4). Or at another firm, referring to collaborators at a US LPC, "they couldn't believe how optimal the situation was here: all the people virtually at one place, [compared with having to] walk into the office and say 'I have to drive nine hours south to Delaware' […] or this and that. So I think one shouldn't underestimate these, as we say in Germany, 'short ways': you can just walk into the office of the chemist who is doing the synthesis, of the tox[icology] person who is looking at your compounds […] it's very important to have the opportunity of this daily exchange, without having to fly or drive anywhere else, but to have the people at one location. And […] just from having been in research for more than twenty years, I think it's one of our great advantages that, […] all the crucial people are here" (GER-PH-5A). Achieving or retaining critical mass is an important consideration in the allocation of resources across multiple sites.

And yet, for the large German companies, being a "global" company means "we need a research centre in the US and in Japan and in Europe. And you choose your location close to major research centres" (GER-PH-6B). Even the smaller firms were not without such ambitions: a manager at GER-PH-4 acknowledged the under-representation internationally of his company's in-house research and foresaw the potential for a strategic merger in the future, preferably "transatlantic" but, if not, in "some major other market – at least France or England".

A fully integrated global R&D model entails close coordination between different sites, information sharing, more rigorous resource allocation, the elimination of unnecessary duplication of resources, and the hope of improved research productivity. As one interviewee noted, "we tended to organise our affairs locally, to suit the local culture. What we found was that in order to be efficient many of our technology platforms and systems needed to go global […] So we had to put in a lot of time building new platforms so that we can exchange information in particular […] About a year ago, there was so much going on we needed to get much more serious about it. So two new posts were created within discovery that were heads of the global disciplines of chemistry and biology – so it was another step, if you like, in the direction of the discovery of the organisation becoming more global" (US-PH-2C). Certain technology-driven 'base' functions and key skills (such as organic chemistry or microbial biology) are increasingly organised to serve all a firm's discovery sites from one or more locations. "For example chemical libraries and high-throughput screening, you know, we have located those in two or three locations, so we prepare the chemical library approach and we do the high-throughput screening and so teams will say, 'we want to look at this particular target' and […] they will liase with the scientists who do that work, and they will work together with them, so there are teams that are coalescing and coming apart and coalescing again" (UK-PH-6A). German firms such as GER-PH-10 and GER-PH-1 espoused similar organisational arrangements.

Although most US firms emphatically claim to have a global drug development organisation, in the majority of cases the current spread of discovery research locations does not yet amount to a fully global strategy. Only a small number of US LPCs have a significant foreign discovery research presence. Whereas some LPCs boast a long history of innovative activity in one or more Triad locations – Pfizer's UK site celebrated its 50th anniversary in 2005, for example – other US firms have in practice focused their discovery research almost entirely in the home country, albeit at several different sites. Some firms are not convinced of the necessity of conducting research overseas. One interviewee even commented with regard to an overseas research site, "It's probably a leftover from previous times. We probably wouldn't do it today' (US-PH-3A). On the other hand, a competitor stressed that it is 'obvious that now and for the future we have to develop drugs in a global manner. It's not good enough that the US says, 'we want to have this drug and don't care about the rest of the world' because the cost of developing a drug globally or regionally is not that different. So why wouldn't you do it globally? And we simply didn't have that capability, and we're still struggling

particularly in Asia – that's an area where we have to invest more to be truly global" (US-PH-5). But the same respondent also confirmed that, in terms of research weighting, his company remains "heavily US-based". Another LPC claimed that their research "will always be centralised in the US but that doesn't in any way impede us from becoming a global company with our products – they can be discovered any place" (US-PH-4) – while nevertheless conceding that the company's low research presence in the other two Triad regions was a potential weakness in terms of accessing knowledge globally (US-PH-4). A third LPC both claims and possesses "a lot of R&D activity in Europe" and in Japan (US-PH-8). Genzyme is a rare example of a large US biotech firm establishing an important overseas facility, in Cambridge UK.

Although European firms believe they can find talented scientists in their home countries, they acknowledge that human exchange between sites is highly desirable. But they regret that such transfers rarely involve Americans relocating to Europe, both for language reasons (in the case of Germany) and for cost reasons. But they also believe themselves to be more immune to knowledge leaks because of the lack of constant job-hopping in Europe, as well as able to achieve a good balance between innovation and continuity. "It is not difficult to get good scientists in [our principal research site] because there are many Europeans with skills [who] would love to work in Europe" (GER-PH-4). A smaller firm found that "in Sweden you can recruit the best talent because they recognise you as a global leader. So rather than trying to compete in the pool of intellect in North America, you are picking up and tend to get the best talent in the country, which I think is an important ingredient" (UK-PH-2A). Many firms commented on relative costs, also: "It's much more cost effective to do [research] in the UK than it is in Boston." (UK-PH-6A), yet the same respondent also admitted that "in many areas of our endeavour it's to the US we have to go for the highest quality people, because the pace of technology is moving and we need to connect to that". Comparing the availability of scientific talent within Europe, "certainly Germany is very good" but the UK is "probably better […] despite the brain drain that everyone goes off to the States" (UK-PH-5). A German LPC respondent expressed concerns over a brain drain to the US unless the government relaxed regulations on gene research: "it's a question of will the government get out of the way […] and limitations on what kinds of research and what fields can we move to" (GER-PH-2A). The centrifugal force of the US pharmaceutical industry with regard to global talent is clearly apparent to US LPCs. "Oh yeah, the brain drain is coming to me. I'm really thrilled… I consider the entire world our recruiting base, even if our operations are here" (US-PH-4); and again, "[This

industry] is about talent. I'm convinced I can, by and large, recruit any talented person, anywhere in the world, to join us in the US" (US-PH-5). An American scientist at a German company's US research facility stated the case plainly: "the US has been entirely successful in just about everything we've done, but most of it has not been done by Americans. Most of the people that we've attracted from other companies either from Europe or from Asia come here to work because of the environment. It's not that we're any smarter, it's just that we're better at providing an environment where these people want to be. And we take advantage of that as a culture. And Germans tend, and other cultures, tend to be more restrictive, and so a bright young scientist with lots of ideas and very few restrictions on where he lives and works can certainly find other places to go" (GER-PH-2A).

Some firms explicitly underline the interplay between their scientists and the local environment. One German firm, having been prevented by German law from entering biotechnology in the late 1980s, is categorical about the reasons for consolidating all of its US research into California: "It's very incestuous, and formal and informal collaborations are entirely common. And that's why you have to be there – you have to be able to plug into that. […] You've got to be a part of the family" (GER-PH-2A). One US LPC that had recently invested in a new research laboratory in the Boston area similarly emphasised the relational advantages of proximity: 'the intention of moving to that area is to gain access to the biotechnology companies and universities that are in that geographical area. And then we actually have learned over the years that physical proximity, even with electronic communications, is really valuable in fostering relationships and much of licensing and external research is relationships' (US-PH-6A). However, not even all US LPCs have a presence in knowledge-laden regions, as Table 1 shows, and indeed, one such company claimed that attendance at the many investment banking, biotechnology and pharmaceutical association meetings, as well as scientific conferences, compensated for its lack of physical presence (US-PH-8).

Smaller firms, both UK and German, observed how difficult it was to break into US networks as suppliers of technology or services unless they had a local presence (GER-PH-7), and even then it was tough to break into longstanding relationships (UK-PH-8). But another German biotech noted that it has formed collaborative relationships with the US labs of two German LPCs, rather than with the home country research sites. This arrangement clearly reflected the impact of the LPCs' reorganisation of their research activity into centres of excellence, and we might speculate that the formation of the relationship with the biotech firm was facilitated by the presence of German

scientists in the US labs. On a broader note, the 'brain drain' of European scientists to the US could offer scope for these people to act as bridges between their US employers and European LPCs or biotechs seeking research collaborations or compound licences.

The importance of a US research site for non-US firms was expressed by all respondents with varying degrees of intensity. One UK firm stated: "We always want to have a presence in the US. Even as a small biotech company, we had one site in the UK, two sites in the US, even though we were UK based, listed on the UK stock exchange" (UK-PH-3). The prime motivation is summed up by the following quote from a German LPC: "In terms of pharmaceutical sciences, biological sciences, the US is the leading source of ideas, the leading country, and you have to be present there. […] You have the top universities in the US, and if you are not present there it is difficult to get contact to them. From here [Germany] it is possible, but it's more difficult" (GER-PH-1A). It signals that a foreign research site may provide the basis for external prospecting for knowledge in the region/country and, reflecting the fact that the US is the only Triad country where firms are actively and deliberately opening new sites, it underlines the institutional advantages of the US highlighted earlier.

In the following section, we turn to an examination of external knowledge sourcing.

III.2 Geographical Aspects of External Knowledge Sourcing

Yoshino and Rangan (1995) contend that, for firms that compete globally, a global network of strategic alliances with external partners now represents a basic building block in innovative activity, rather than a simple means of plugging well-defined competence gaps. For vertically integrated pharmaceutical firms, external sourcing is a complementary innovation strategy rather than a substitute for internal research, since the requisite skills to evaluate external knowledge need to remain in-house. LPCs form research partnerships with smaller pharmaceutical firms and biotechs (and, at a very early stage in the discovery process, also academic research institutions), but the balance of power in relationships with external knowledge providers is shifting away from a one-sided dominance of LPCs to a more equal relationship with biotech firms because of the dearth of compounds available for in-licensing (Lane and Probert 2005).

The geographic focus of selecting research partners may be embedded in historical attempts to overcome national institutional weaknesses. According to Senker and Sharp (1997), German LPCs in the 1980s and early 1990s showed a propensity to

develop links with both local universities and US biotech firms (because domestic impediments had prevented the emergence of a national biotechnology industry), whereas they found that the more vibrant biotechnology community in the UK encouraged LPCs there not to overlook ties with either local universities or local biotechs; meanwhile US biotechs looked mainly to forge partnerships with US LPCs. But our data suggest that this picture has changed for both German and UK LPCs, although not for US LPCs. As a result of the 1996 BioRegio initiative, biotech firms have sprung up in various clusters around Germany, some with a strongly transatlantic perspective, and these present greater opportunities than previously for LPCs to engage in local partnering. German LPCs with strong research bases in the US now have opportunities to collaborate with both US partners and domestically based biotechs. British LPCs, on the other hand, acknowledge their tendency to form ties as much, if not more so, with American biotech firms as with British partners, reflecting the possible influence of their heavy in-house research weighting in the United States.

Despite concern expressed over the increased bargaining power of US biotechs and the high prices they are able to command for new compounds, as well as dissatisfaction with the behaviour of US academic institutions (Lane and Probert 2005), for US LPCs the pull of the US remains. As one Europe-based scientist with a US firm explained, the search for external partners is "not organised regionally, it is organised therapeutically. If you take [his therapeutic area, for which responsibility lies in Europe], that team would be responsible worldwide for opportunities, some of which might be from European-based companies, some will certainly be from US-based companies. A lot of activity would be in the biotech sector, and of course the US has a much more highly developed biotech sector than we do in Europe" (US-PH-2C). Theoretically, at least, members of this team would travel the world. A US-based respondent in the same LPC confirms "Yes absolutely, [we license from any geographical location], it doesn't matter" (US-PH-2B). In contrast, another respondent in this company declares "you've got to be where the action is, and most of the action is in the US. Europe has really fallen off the scale as well [as Japan]' (US-PH-2A). Reflecting the dominance of the US industry, another US LPC based the majority of its licensing team in the US and employed only two business development people in Europe (US-PH-3B). Prospecting in Japan – which was recognised to be important – was managed by regular visits from US-based members of the team because of the expense of locating an expatriate there.

One UK firm claims to pursue a genuinely global licensing strategy: "we have a licensing organisation that broadly sits in the development box, which is global, with

people in Japan, the States and Europe – just looking at opportunities" (UK-PH-6A). Our analysis of its in-licensed product/compound portfolio concurs with this representation. Another UK firm agreed that most of its licensing activity is in the US, and notes that it has been active in seeking opportunities, "partly to fill the pipeline, but it was also partly to produce a bit of creative tension in the whole process. And […] although we've done a great job on [our] R&D, we just wanted to spread the bet a little bit" (UK-PH-4A). A third, while prospecting widely for particular technologies – but mainly in Europe and the US – prefers to capture competences and synergies through acquisition because "collaborations don't normally endure management change" (UK-PH-2A).

For the smaller firms in our German sample, lack of marketing muscle impedes their ability to compete for compound in-licences, as one respondent explains: "it is easier for us to give licences as we have rather good research and, compared to this, we do not have the power in place to do the selling ourselves. […] If we look for in-licences, we want to have at least a transatlantic deal, North America included, [… but] the big companies which have a demand for products are good addresses for licensed products. […] But of course we would be happy to have some in-licensed products" (GER-PH-4). On the other hand, this same firm has forged a long-lasting research relationship with a German biotech where the actual activity (into genomics and proteomics) is conducted in the United States. A five-year genomics-related alliance with a US biotech firm was one of the "major drivers" behind another German firm's efforts to catch up in technologies where it was lagging (GER-PH-6B). Since government constraints until relatively recently prevented the accumulation of genomics-related knowledge in Germany, German firms look to the main source of technology – the US – rather than elsewhere in the world in order to overcome their disadvantage. But one German biotech also argued forcefully that, because it found no relevant research being done in the US, "we are collaborating with groups who can provide the extra intellectual input and protection in our fields of interest. And therefore, not surprisingly, that's Euro-centric, not US-centric" (GER-PH-3).

Whether or not they aspire to 'global' research organisations, firms organisationally manage their prospecting and decision-making structures for collaborations separately from their compound in-licensing activities. Not least, the financial commitments involved are of a different order entirely. At the research or technology collaboration level, some firms devolve to the therapeutic area level, or to the research discipline, responsibility for identifying potential partners. Authority to

enter into a partnership then depends on the expenditure involved and the level of autonomy accorded to the unit. One UK interviewee told us that in his firm "the people who form [the technology acquisition] group are actually the people who use the technology, whereas […] I know from my own experience at [another UK LPC], a different group of people look for the technologies than those who actually use the technologies" (UK-PH-1). Decentralised research sites thus appear to be more important conduits for the diffusion of external knowledge at some firms than at others. For compound licensing, some firms (e.g. GER-PH-1) have distributed staff across their major sites, with international evaluation teams to assess potential projects against standardised criteria. Reporting structures for licensing teams vary, with some LPCs' teams reporting to the board, while others are housed within the R&D organisation and answer to the R&D director. But whether business development/licensing teams are centrally located or dispersed across the firm's network, the final decision on whether or not to in-license is made at headquarters, at very senior levels of authority. Especially in the case of expensive late stage compounds, the financial risk to the firm is large and must be weighed up against other possible options.

In their relationships with academic institutions, both pharmaceutical firms and biotechs rely more heavily on personal connections than is the case with company-to-company research collaborations or licensing agreements, as other scholars have noted (e.g.Chiesa and Manzini 1997). This suggests a possible bias towards relationships with academia in the same country as the home research laboratory, particularly if the firm's research is relatively centralised. All the firms we interviewed had connections with at least one university, and indeed one firm (GER-PH-1) funds a research institute specifically to act as its bridge with academia. That respondent noted a strong relationship with a German research institute where some of his university friends worked, "and that's important, long relationships: you can trust those people and that is important in the early [stage]". One firm recognised that "in reality, [agreements] should not focus on these personal strings, but should be driven by technology, research, new products, patents etc." (GER-PH-6A). Although US university linkages are more likely to dominate US LPCs' lists than the geographically more diverse lists of European LPC collaborations, one US LPC stated, "We go where we believe the science is the best – the individual lab – where the best laboratory or company in a given area would be. We don't limit ourselves geographically" (US-PH-6). A Europe-based interviewee in another US LPC claimed that 'one of the things we do quite well is look for relationships with organisations outside of the conventional US blue-chip academic

institutions. So actually we do have a number of significant collaborations with major centres around Europe particularly' (US-PH-3B). According to its website (accessed 21 March 2004), GSK has more than 800 early stage discovery collaborations with colleges and universities around the world, and other LPCs, too, stress in their public materials the wide range of academic collaborations they have forged around the world.

Our analysis of the database of the national origin of licensed compounds and collaborations that we constructed for eight US, two UK and six German LPCs broadly supports the views expressed by our interviewees. A summary of the database is presented in Table 2.

Table 2: Externally sourced knowledge by region - compounds, candidates and collaborations

a) for 8 leading US LPCs

	US	W. Europe	Japan	RoW
Marketed compounds*	31.5	23.5	19	1
Pipeline candidates**	47.5	19.5	8	1
Biotech collaborations***	162.5	47	0	11.5

b) for 2 UK LPCs

	US	W. Europe	Japan	RoW
Marketed compounds*	5	5	5	0
Pipeline candidates**	25	3	8	1
Biotech collaborations***	52	26	0	2

b) for 6 German LPCs

	US	W. Europe	Japan	RoW
Marketed compounds*	10	1	3	0
Pipeline candidates**	13	11	4	0
Biotech collaborations***	48	46	0	4

* Compounds in-licensed at some stage of development that are now on the market. Excludes products that enter a company's drug portfolio as a result of M&A activity.
** Excludes products that enter a company's drug portfolio as a result of M&A activity.
*** Compound or technology agreements reached with biotechnology companies and universities in a 30-month period to 10/04.

Source: own calculations, derived from database constructed from multiple sources.

Whereas both Europe and Japan have been good hunting grounds in the past for US LPCs' in-licensing activity, as measured by the provenance of drugs already on the market, Japan has been the source of noticeably fewer compounds in development in more recent years while US firms seem to be providing more candidates. This picture is intensified when we examine the geographic spread of recent collaborations with

biotechnology companies and universities. Here we find that US LPCs are three times more likely to have found US biotech partners than European partners, and that none of our US LPCs had signed an agreement with a Japanese biotech firm during the 30-month period covered by this line of our data. Nor was Japan an attractive source of biotech collaborations for either UK or German firms, reflecting the immaturity of the sector in Japan, although UK firms had more drugs in the pipeline of Japanese than of European origin. These compounds came from medium-sized Japanese firms that lacked substantial infrastructure outside their home market.

But in most other respects Table 2 underlines the marked differences in external knowledge sourcing strategies between British and German LPCs that our qualitative data indicate. Although firms in both countries formed relationships with European biotechs and research institutes, the British LPCs demonstrated a significant bias towards the US for discovery compounds and technologies. With respect to *pipeline* candidates they were also more likely to look outside their home region, to both the US and Japan, than their German counterparts. And, on average, each UK firm signed many more deals than a German LPC, even taking into account the greater size of the UK LPCs, at all levels of the research and product portfolio. The underlying (unaggregated) data show that the US and UK LPCs have similar levels of in-licensed marketed products, but German firms uniformly have fewer such drugs. The preponderence of *marketed* drugs in-licensed by German firms, however, come from US LPCs and may not carry worldwide rights. At the pipeline level the picture is more mixed, with a couple of the larger German firms behaving more like the majority of their US/UK counterparts by sourcing actively from outside while the rest remain firmly focused on in-house research activity. But the more active German external sourcers are just as likely to find compounds in Europe as in the United States, unlike the US and UK firms. Finally, the data support our qualitative findings with respect to increased interest among the German firms to develop collaborations with biotech companies, although here again we find two firms with very limited external partnerships and, overall, more balanced portfolios of activity with European and US biotechs and universities.

Conclusion: Global Internal and External Knowledge Networks?

The preceding sections have discussed geographical trends in LPCs' internal and external knowledge sourcing. But can their knowledge sourcing practices be described genuinely as global strategies? US LPCs have been shown to act opportunistically in their licensing activity, whatever their stated intentions with regard to therapeutic areas of focus (Lane and Probert 2005). Such opportunism could broaden the geographic spread of the partnerships that firms form, particularly if their business development teams have a genuinely global remit. But our research shows that, whereas most firms espouse a general belief about the importance of a local presence and/or research network, many American and European firms actually operate within a more constrained geographic sphere. This may be for cost reasons, e.g. the expense of locating specialist prospecting staff in countries such as Japan, or a strategic decision to concentrate limited resources in known 'hot' regions for technology. It could also – although this was not explicitly stated during any of our interviews – be due to discomfort in negotiating with prospective partners from an unfamiliar institutional or national environment.

Several US LPCs claim to pursue an active global knowledge-sourcing strategy, although in practice much of their activity is driven by, and occurs in, the US. There is considerable organisational decentralisation of the R&D function, as shown in Table 1, but for US LPCs this occurs mainly within the home country. The huge costs of running sizeable R&D sites in Europe and/or Japan act as a deterrent for some firms, unless these operations have already been shown to be productive. One US LPC threatened to relocate a European research site unless it accepted sweeping organisational changes and improved its performance, which it did (US-PH-5). Another said that it would scale back operations in Japan before cutting back in Europe. But there was no sense of a need to rebalance the spread of in-house research away from the US. The picture on external knowledge providers revealed in Table 2 is similarly firmly weighted towards the US, particularly at the early, collaborative stages of research. This is natural, since there are many more prospective partners in the US biotechnology industry than in any other country. (Many of the marketed drugs orginating in Europe came from LPCs, rather than biotechs, reflecting the relative immaturity of the European biotech industry a decade ago.) However, the underlying data show that three of the four US LPCs that formed 25 percent or more of such alliances with European firms are those with significant research sites in Europe. This suggests that some form of bridging

mechanism may be at work. Notwithstanding an earlier quotation regarding teams from an overseas laboratory prospecting for partners worldwide, locally embedded scientists are more likely to have a keener understanding of local and national research trends and capabilities than distantly located colleagues.

For UK and German firms the geographical picture is more varied, principally because of the US's magnetic pull away from the home base in Europe. But for none of these firms does their Japan unit attain the importance of their US and European research sites – despite praise for the science conducted there – and they cannot therefore be described as operating genuinely global research networks. It is clear that UK firms are more US-oriented than the majority of German firms, both in terms of in-house research and research collaborations, although internal and external innovation activity in Europe continues to represent an important source of research diversity. (They are also more US- than UK-oriented, which is logical given the disparities in number of potential biotech partners and does not mean that the UK biotech base is not valued.) Turning to the data for German firms, those with more substantial (and older) research bases in the US tend to form a higher proportion of collaborations in the United States than those with more limited overseas research activity. This suggests that embeddedness in the local environment does indeed play a role in facilitating cooperative research and that this is likely to intensify.

But both UK and German LPCs were clear that the quality of the available inputs is the driving force behind their geographical sourcing practices. As one German respondent expressed it: "we are all obliged to think globally, we have to, and we also want to – we have to – go for the best things out there. And this must be independent – I don't interact with somebody for example here [in Germany] simply because he or she is close; I want to interact with the person who is best, and if this person is in Stanford, then I will interact with them in Stanford. And that's what people have to understand: there's no compromise around quality" (GER-PH-10). Challenged to explain why his company spends relatively little of its total partnerships investment close to the home base, this scientist says "I tell them, 'look guys, if you would be better, we would maybe invest some of this money here, but we have to go for the best partner on a global basis. So you are not competing with your neighbour, but you are competing with company X, Y, Z in Great Britain and in the US and in France'" (ibid). Geographical proximity is a less compelling argument for cooperation than the quality of the technology or research on offer.

Whereas it is hard to claim that any firm has a genuinely global knowledge sourcing strategy, many firms are making increasing efforts to integrate their activities and harmonise procedures to a global standard. These efforts operate at two levels. First, it makes sense for certain resources (e.g. high throughput screening, or various aspects of biological science) to serve the entire research organisation, but to function efficiently their processes and output have to be standardised so that work can be performed by one unit or another without interrupting later scientific work because of inconsistencies. Second, all firms in our interview group now aim for international product registration (marketing), requiring harmonisation of development activity and uniformity of standards to a globally high level. Particularly where firms had previously allowed research sites to behave rather independently, practices might vary widely. One firm (GER-PH-1) gave the example of different sites using different animal species to conduct toxicology studies, which meant that one unit could not take some of the heavy workload of another. Such inconsistencies have now been swept away.

Finally, integrating global R&D activities may work at the level of efficiency yet it has its own drawbacks, as one respondent indicates: "a worldwide-aligned organisation is a very useful conceptual and organisational construct for getting things done, but in terms of engaging people and motivating people it's not very powerful. It's too abstract and too far away" (US-PH-2C). Engagement and motivation remains at the local level, but work takes place increasingly at the project team level. Finding a way to stimulate active cooperation across geographically dispersed teams probably remains one of the greater challenges for LPCs.

As to longer term trends in LPCs' in-house R&D location choices, the following quotation from an interviewee well sums up our view: '… I would be willing to bet, if there is an expansion of R&D by American companies or by European companies, that the vast majority will be in the US. My counterparts, and I know them all, who head R&D… every company, any of them contemplating expansion now or in the future are thinking of the US. I think it's bad for Europe, but I also think it's a fact and it's already started' (US-PH-4). Not only, therefore, is the US a more likely location for US LPCs to source new technology and ideas, and new drug candidates, but it is also attracting European pharmaceutical companies' research activities away from their home locations. In these circumstances, there is perhaps not a pressing need for US firms to organise their research activities globally, whereas European firms find themselves almost forced to establish research activity in order to participate in, and embed themselves into, the dynamic US biotechnology environment.

Notes

[1] An earlier strategy by US and UK firms to focus on pharmaceuticals/life sciences also helped them to grow faster than their more diversified German competitors.

[2] For the purposes of this paper we ignore technology licences.

[3] The shareholder-value driven strategy of its management took the company through several mergers in the 1990s, becoming Aventis in 1999 and Sanofi-Aventis in 2004.

[4] Between 1990 and 1999, EU pharmaceutical firms' R&D spending inside the EU fell from 73 percent to 59 percent, while the proportion conducted in the US rose from 26 percent to 34 percent (EFPIA, 2002), against a background of rising absolute R&D expenditure.

[5] Hoechst represents a notable example of a large firm violating this principle, and Bayer's recent reorganisation indicates similar disregard for social norms.

References

Aitken, M., S. Baskaran, E. Lamarre, M. Silber and S. Waters (2000), 'A license to cure' in *McKinsey Quarterly* No.3, pp.80-89.

Bartlett, C. A. and S. Ghoshal (1989), *Managing Across Borders: The Transnational Solution* (1st ed.), Boston: Harvard Business School Press.

Becker, S. (2001), *Einfluss und Grenzen des Shareholder Value: Strategie- und Strukturwandel deutscher Grossunternehmen des chemischen und pharmazeutischen Industrie*, Frankfurt: Peter Lang.

Blanc, H. and C. Sierra (1999), 'The internationalisation of R&D by multinationals: a trade-off between external and internal proximity' in *Cambridge Journal of Economics*, Vol.23, pp.187-206.

Booth, B. and R. Zemmel (2004), 'Prospects for productivity' in *Nature Review Drug Discovery*, Vol.3, pp.451-457.

Buxton, B.R. and R.J. Easton (2003), 'Blockbusters to new-engine drugs: the key industry shift' in *In Vivo: The Business and Medicine Report* July/August: 63-70.

Cantwell, J. (1998), 'The globalization of technology: what remains of the product cycle model?' in A. D. Chandler, P. Hagström and Ö. Sölvell (eds.), *The Dynamic Firm: The Role of Technology, Strategy, Organizations, and Regions*, Oxford: Oxford University Press.

Cantwell, J. and J. Molero (eds.) (2003), *Multinational Enterprises, Innovative Strategies and Systems of Innovation*, Cheltenham: Edward Elgar.

Casper, S. and H.E. Kettler (2001), 'National institutional frameworks and the hybridization of entrepreneurial business models: the German and UK biotechnology sectors' in *Industry and Innovation*, Vol.8, pp.5-30.

Castilla, E.J., H. Hwang, E. Granovetter and M. Granovetter (2000), 'Social Networks in Silicon Valley' in C.-M. Lee, W. F. Miller, M. G. Hancock and H. Rowen (eds.), *The Silicon Valley Edge: A Habitat for Innovation and Entrepreneurship*, Stanford CA: Stanford University Press.

Chiesa, V. and R. Manzini (1997), 'Managing virtual R&D organisations: lessons from the pharmaceutical industry' in *International Journal of Technology Management*, Vol.13, No.5/6, pp.471-485.

de Rond, M. (2003), *Strategic Alliances as Social Facts*, Cambridge: Cambridge University Press.

Edler, J. (2004), 'International research strategies of multinational corporations: a German perspective' in *Technological Forecasting & Social Change*, Vol.71, pp.599-621.

EFPIA (2002), 'The Pharmaceutical Industry in Figures – 2002 Edition', Brussels: European Federation of Pharmaceutical Industries and Associations.

EFPIA (2005), 'The Pharmaceutical Industry in Figures – Key Data: 2005 Update', Brussels: European Federation of Pharmaceutical Industries and Associations.

Ernst & Young (2003a), 'Endurance: The European Biotechnology Report 2003', Cambridge: Ernst & Young.

Ernst & Young (2003b), 'Resilience: Americas Biotechnology Report 2003', Ernst & Young.

Faust, M. , Ulrich V. and Volker W. (2004), 'Globalization and the Future of National Systems: Exploring Patterns of Industrial Reorganization and Relocation in an Enlarged Europe' in M. Faust, U. Voskamp and V. Wittke (eds.), *European Industrial Restructuring in a Global Economy: Fragmentation and Relocation of Value Chains*, Goettingen: Soziologisches Forschungsinstitut Goettingen.

Florida, R. (1997), 'The globalization of R&D: results of a survey of foreign-affiliated R&D laboratories in the USA' in *Research Policy*, Vol.26, pp.85-103.

Frost, T.S., J.M. Birkinshaw and P.C. Ensign (2002), 'Centers of excellence in multinational corporations' in *Strategic Management Journal*, Vol.23, pp.997-1018.

Gerybadze, A. and G. Reger (1999), 'Globalization of R & D: recent changes in the management of innovation in transnational corporations' in *Research Policy*, Vol.28, pp.251-274.

Hall, P. A. and D.W. Soskice (2001), *Varieties of Capitalism: The Institutional Foundations of Comparative Advantage*, Oxford: Oxford University Press.

Hemmert, M. (2004), 'The influence of institutional factors on the technology acquisition performance of high-tech firms: survey results from Germany and Japan' in *Research Policy*, Vol.33, pp.1019-1039.

Hicks, D. (1993), 'University-industry research links in Japan', in *Policy Sciences*, Vol.26, pp.361-395.

Lane, C. and J. Probert (2005), 'The external sourcing of technological knowledge by US pharmaceutical companies: strategic goals and inter-organisational relationships', unpublished manuscript, Cambridge: University of Cambridge.

Lehrer, M. and K. Asakawa (2003), 'Managing intersecting R&D social communities: a comparative study of European 'knowledge incubators' in Japanese and American firms' in *Organization Studies*, Vol.24, No.5, pp.771-792.

Lehrer, M. and K. Asakawa (2004), 'Rethinking the public sector: idiosyncracies of biotechnology commercialization as motors of national R&D reform in Germany and Japan' in *Research Policy*, Vol.33, pp.921-938.

McKelvey, M. and L. Orsenigo (2001), 'Pharmaceuticals as a sectoral innovation system', Vienna: paper presented at the European Meeting of Applied Evolutionary Economics.

Milken Institute (2004), *Biopharmaceutical Industry Contributions to the States and US Economies*, Santa Monica, CA: Milken Institute.

Nelson, R.R. (Ed.) (1993) *National Innovation Systems: A Comparative Analysis*, New York: Oxford University Press.

OECD (2004), 'Science, Technology and Industry Outlook', Paris: OECD.

Owen-Smith, J., M. Riccaboni, F. Pammolli and W.W. Powell (2002), 'A comparison of U.S. and European university-industry relations in the life sciences' in *Management Science*, Vol.48, No.1, pp.24-43.

Pearce, R. (1999), 'Decentralised R&D and strategic competitiveness: globalised approaches to generation and use of technology in multinational enterprises (MNEs)' in *Research Policy*, Vol.28, pp.157-178.

Pearce, R. and S. Singh (1992), *Globalizing Research and Development*, Houndmills: Macmillan.

Powell, W.W., K.W. Koput and L. Smith-Doerr (1996) 'Interorganizational collaboration and the locus of innovation: networks of learning in biotechnology' in *Administrative Science Quarterly*, Vol.41, pp.116-145.

Powell, W.W., D.R. White, K.W. Koput and J. Owen-Smith (2005), 'Network dynamics and field evolution: the growth of interorganizational collaboration in the life sciences' in *American Journal of Sociology*, Vol.110, No.4, pp.1132-1205.

Reger, G. (2000), 'Internationalisation strategies of selected pharmaceutical companies' in A. Jungmittag, G. Reger and T. Reiss (eds.), *Changing Innovation in the Pharmaceutical Industry: Globalization and New Ways of Drug Development*, Berlin: Springer.

Senker, J. and M. Sharp (1997), 'Organizational learning in cooperative alliances: some case studies in biotechnology' in *Technology Analysis & Strategic Management*, Vo.9, No.1, pp.35-51.

Storper, M. and R. Salais (1997), *Worlds of Production : The Action Frameworks of the Economy*, Cambridge MA: Harvard University Press.

Taggart, J. (1991), 'Determinants of the foreign R&D locational decision in the pharmaceutical industry' in *R&D Management*, Vol.21, pp.229-240.

Von Hippel, E. (1999), '"Sticky information" and the locus of problem solving : implications for innovation', in A. D. Chandler, P. Hagström and Ö. Sölvell (eds.), *The Dynamic Firm: The Role of Technology, Strategy, Organization, and Regions*, Oxford: Oxford University Press.

Yoshino, M and U.S. Rangan (1995), *Strategic Alliances: An Entrepreneurial Approach to Globalization*, Boston, MA: Harvard Business School Press.

Zeller, C. (2001), 'Clustering biotech: a recipe for success? Spatial patterns of biotechnology in Munich, Rhineland and Hamburg' in *Small Business Economics*, Vol.17, pp.123-141.

Zeller, C. (2004), 'North Atlantic innovative relations of Swiss pharmaceuticals and the proximities with regional biotech arenas' in *Economic Geography*, Vol.80, No.1, pp.83-111.