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The globalisation of research amongst leading European and US pharmaceutical
multinationals: The shift of European investment to the USA

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Abstract:

The paper examines evidence from three types of data to gauge the globalisation of research in the pharmaceutical industry. The results show a flow of European investment to the USA with no corresponding investment flow from the USA to Europe. Rather than globalisation the results show the increasing 'Americanisation' of research in this industry. The data indicate that it is not only the leading-edge nature of science and technology that is pulling R&D towards the USA but also the size and dynamism of the US market and an institutional system which allows relatively easy access to academic research.

Keywords: Globalisation, Innovation, Pharmaceutical Industry, Foreign Direct Investment, Technological-alliances

1. Introduction

Over the last decade, the extent and character of trends towards the internationalisation and globalisation of innovative activities have been subjects of lively debate. Underlying this discussion are deep concerns as to whether the establishment of R&D activities abroad weakens the technological potential and competitiveness of the home countries (ETAN 1998). Similarly, the ability of countries to attract foreign investment either via foreign direct investment (FDI) or the investment implicit in technological collaborations and the impact of this on their scientific and technological infrastructure are issues of concern. More recently, increasing awareness has begun to surface about a widening gap between Europe and the USA and Japan in the most dynamic sectors of the economy, above all in ICT (Archibugi and Coco 2001; Fagerberg 2001).

The debate on the globalisation of innovation centres on a number of issues including: the extent of the internationalisation and globalisation of innovative activities; the character of the innovative effort performed abroad; as well as the factors and motivations behind the international location of research activities. To a large extent this debate reflects the uneven, complex, and often contradictory nature of the process of internationalisation of innovative activities. Nevertheless the existence of different conceptualisations of the term 'globalisation' has added an extra layer of complexity to the discussion.

The present paper sets out to examine the evidence relating to the 'globalisation of innovation' in the pharmaceutical industry. Five dimensions of the process of

internationalisation and globalisation of innovative activities are examined, namely: The percentage of the research effort performed outside the country of origin of multinational corporations (MNCs); the geographical spread of the MNC's innovative facilities; the importance of the international research activities to the overall innovative effort of the MNC; the growth and importance of cross border technological alliances in the innovative strategy of firms; and the existence of an international division of labour in R&D along with the degree of integration and coordination of a MNC's international research effort. The five dimensions are examined using three types of data: The US patenting activity of fifteen leading European and US pharmaceutical multinationals; data on cross-border technological collaborations in the pharmaceutical industry; and data collected from interviews with senior managers within the R&D function from nine pharmaceutical companies. The paper goes on to discuss the motivations behind the globalisation of research activities.

The paper is organised as follows: section 2 refers to the debate which has taken place during the 1990s on the extent and characteristics of the globalisation of innovation and specifies five major dimensions of this process. Section 3, discusses the globalisation of innovation in the pharmaceutical industry. Section 4, reports the results of data from US patents, cross-border technological alliances and interviews with senior research managers in a sample of European and US multinational corporations analysed to gauge the extent and nature of the process of globalisation of innovation in the pharmaceutical industry. The forces motivating the globalisation of innovative activity in this industry are discussed in section 5. Section 6, concludes the discussion

2. Conceptualisations of “globalisation of innovation”

One very influential current of opinion in the debate on the globalisation of innovation has been the work of Patel and Pavitt (Pale and Pavitt 1991, 1998; Patel 1995; Pavitt and Patel 1999) who have conceptualised the ‘globalisation of innovation’ as the percentage of research and development (R&D) activities performed by firms outside their country of origin. The geographical spread of the innovative effort of large multinational firms is another important dimension of the process of globalisation in these works. On the basis of empirical evidence provided by US patent data these scholars argue that the globalisation of innovation is not taking place, though it is acknowledged that the pharmaceutical industry is more internationalised than others.

Another current of opinion (Cantwell 1992, 1995; OECD 1992, Chesnais 1992; Pearse 1999) has made a distinction between the ‘internationalisation’ and the ‘globalisation’ of innovative activities. By internationalisation these authors mean the proportion of innovative activities performed outside the country of origin of firms (what Patel and Pavitt have termed globalisation). The globalisation of innovation, on the other hand, is conceptualised as the existence of an international division of labour in R&D and a greater degree of international coordination of innovative facilities by multinational enterprises. A further stream of research has focused on the growth of cross-border technological collaborations as evidence of the growing globalisation of innovation (Mytelka 1990, 1999; Hagedoorn 1994, 1995; Miotti and Sachwald 2003).

The rise of international intra and inter-firm R&D networks are therefore at the heart of these conceptualisations of globalisation of innovation (Dunning 1997). A number of indicators, including US patent data and cross-border technological alliances, have been used to analyse the degree of globalisation of innovative activities. On the basis of these data a number of scholars have concluded that though the majority of firms' R&D activities continues to be located in their country of origin, multinational corporations (MNCs) are globalising their innovative efforts by developing an international division of labour between geographically dispersed research sites (Cantwell 1995; Dunning 1994; Pearce and Singh 1992; Pearce 1999). At the same time, a number of industries have seen a qualitative increase in the numbers of cross-border technological alliances (Hagedoorn 1995; Miotti and Sachwald 2003).

What this debate has highlighted is that there are in fact a number of different dimensions to the process of globalisation of innovation which have developed in complex, uneven and sometimes contradictory ways. In this paper the defining feature of the 'globalisation of innovation' is the existence of international integrated intra and inter-firm research networks. There are however, a number of dimensions to this process (including high degrees of internationalisation) the most important of which are:

1. The percentage of the research effort performed outside the country of origin of the MNC;
2. The geographical spread of the MNC's innovative facilities;
3. The importance of the international research activities to the overall innovative effort of the MNC;

4. The growth and importance of cross border technological alliances in the innovative strategy of firms.
5. The existence of an international division of labour in R&D and the degree of integration and coordination of an MNC's international research effort.

All five dimensions are important aspects of the process of globalisation of innovation; nevertheless the key difference between the internationalisation and globalisation of this activity is the existence of a coordinated international division of labour in research.

The debate about the extent and nature of the globalisation of innovation has also shown that a complex set of factors have a bearing on the globalisation of innovative activities by MNCs. On the one hand, the globalisation of innovation is part of a much broader process of economic, institutional and technological change (Chesnais *et al* 2000; Lundvall and Borras 1997; Dunning 1997; Mytelka 1999; Howells 1990 a,b). On the other hand, important issues pertaining to the character of the process of technological innovation provide both a stimulus and set limits to the international dispersal of firm's R&D activities. The need to access science and technology developed outside the home country has been highlighted as one of the main motivations for the globalisation of innovative activities in a period of radical technological change (Pearce 1989, 1999; Cantwell 1992, 1995; OECD 1992; Gerybadze and Reger 1999). Survey data also shows the importance of locating close to 'customer-related pools of knowledge' and advanced users in most industries (Gerybadze and Reger 1999).

Innovation scholars however have also pointed to factors related to the very nature of the process of technological innovation as limiting forces to the possible geographical dispersal of firm's R&D activities (see for example Granstrand 1982). The work of Patel and Pavitt (Patel and Pavitt 1991, Pavitt and Patel 1999) has pointed to the important role of tacit knowledge and economies of agglomeration as a serious limitation to the geographical dispersal of activities of technological creation. At the same time the cumulative and path-dependent nature of learning and searching has been raised as an important force binding the firm's technological activities to its country of origin (Patel and Pavitt 1991, Pavitt and Patel 1999). As a result even scholars who argue that the globalisation of innovation is taking place maintain that the competitive advantage of large firms are still fundamentally linked to their home base (see for example Cantwell 1995 and Cantwell and Janne 2000).

3. The Globalisation of innovation in pharmaceuticals

Since its beginnings the pharmaceutical industry has had a relatively international character with high levels of international trade and foreign direct investment (FDI) in terms of clinical trials, marketing, production and packaging facilities. As is the case with other industries, however, before the 1970s the proportion of research performed outside the home country was relatively small (Dunning 1988). More recent evidence indicates that from the mid-1980s the proportion of research activity performed outside the home country by pharmaceutical firms has increased (Jungmittag *et al* 2000). Opinions still differ, however, as to the degree of internationalisation of the industry's R&D activities. According to some authors pharmaceutical R&D remains relatively centralised in the home country with the most sensitive and demanding

work located in the country of origin (Tarabusi and Vickery 1998). These authors also recognised, however, that as a result of merger and acquisition activities and cross-border technological collaboration there has been an increase in the internationalisation of these activities. Others argue that the process of internationalisation is quite advanced in the industry (Jungmittag *et al* 2000; Taggart 1993; Howells 1990a,b).

Despite differences about the scale of trends towards the internationalisation and globalisation of research, the existence of flows of European pharmaceutical investment towards the USA, spurred by the developments in biotechnology and information technology (IT) in that country, have been well established (Sharp 1996; Sharp and Galimberti 1993; Walsh and Galimberti 1993). The advanced nature of US scientific research in these two areas along with the existence of specialist research and technology companies, the dedicated biotechnology firms (DBFs), as vehicles to access the US academic base has made this country a particularly attractive location for research. The importance of these new technologies for the research process of pharmaceutical firms has meant that much of the innovation literature has focused almost exclusively on the importance of technological change, and the favourable conditions for their development and commercialisation in the USA, as the main factors driving foreign direct investment in research into that country.

A reading of the history of the industry however gives a slightly different picture. For example, in the case of the UK firm Glaxo, Jones (2001) stresses the importance of the US market (and the success of the firm's drug Zantac in that market) in the decision to set up research activities in that country in 1984. The research unit created

as a result of this investment formed the basis for Glaxo's move towards biotechnology some years later (Sharp and Patel 1996). The success of Zantac in Italy was also behind the decision to set up a research laboratory in that country. The importance of dynamic markets for the location of research facilities in the pharmaceutical industry is also supported by research by Taggart (1991) and (Jungmittag *et al.* 2000) (see also Wash *et al.* 2000).

The countries within Europe that have attracted foreign direct investment in research from pharmaceutical firms include the UK and France. In the case of the UK a number of reasons have been suggested to explain the flow of inward investment. These include: a very strong scientific community and good higher educational facilities; a generous pricing system which actively encourages foreign companies to expand their local activities; strict but flexible regulatory controls and a moderate drug market (Sharp and Patel 1996). In the case of France it has been suggested that the explanation resides in the fact that successive administrations have put considerable pressure on foreign-owned MNCs to maximise the value-added component of their local operations. Also despite the fact that drug prices are low the French pharmaceutical market is a large one (Dunning 1988). It is interesting that Germany has attracted little attention from foreign MNCs despite the fact that German chemistry has had an excellent reputation, the internal market is the largest in Europe, and the regulatory environment is benign.

Along with FDI, the move towards greater internationalisation of technological innovation in the pharmaceutical industry has been through an increasing number of cross-border collaborative alliances both with academia and with specialist research

firms in the areas of biotechnology and bio-informatics. In the early 1980s European multinationals such as Ciba-Geigy, Hoffmann-La Roche and Hoechst broke with tradition and placed a number of research contracts with US dedicated biotechnology firms (DBFs). In 1981, for example, the German firm, Hoechst placed a \$67 million 10- year contract with the Massachusetts General Hospital (MGH) on biotechnology which included a training programme for its staff (Kenney 1986). A number of databases such as *Bioscan*, Merit's CATI database and Jungmittag *et al.* (2000) show that in the 1990s in the area of pharmaceuticals the number of biotechnology alliances had experienced considerable growth. By the mid-1990s data on technological alliances showed the deep penetration of the US biotechnology base by European pharmaceutical firms (Jungmittag *et al.* 2000).

The above discussion shows that though there is evidence which points to an increase in the internationalisation and globalisation of innovative activities in the pharmaceutical industry differences still remain about the scale, importance and nature of this investment. The literature also indicates that the role of demand factors in the process of internationalisation and globalisation of the research activities of pharmaceutical firms has received little attention from innovation scholars. The next section examines empirical evidence on the extent, nature and motivation of the internationalisation and globalisation of research in pharmaceutical.

4. Five Dimensions of the Globalisation of Innovation Amongst Leading Pharmaceutical MNCs.

This section reports results on three types of data gathered to gauge the extent and motivation behind the globalisation of innovation amongst leading European and US pharmaceutical MNCs. As discussed in section 2, in this paper the defining feature of ‘globalisation’ as against the ‘internationalisation’ of innovation is the existence of international integrated intra and inter-firm research networks. There are however, five important dimensions to this process, namely: (i) the percentage of the research effort performed outside the country of origin of the MNC; (ii) the geographical spread of the MNC’s innovative facilities; (iii) the importance of the international research activities to the overall innovative effort of the MNC; (iv) the growth and importance of cross border technological alliances in the innovative strategy of firms; and (v) the existence of an international division of labour in R&D and the degree of integration and coordination of an MNC’s international research effort.

The data is both quantitative and qualitative and is used to analyse the extent and nature of the process of globalisation of innovation along the five dimensions. The data consist of: (i) the US patenting activities of a sample of fifteen of the top twenty world pharmaceutical firms for the period between 1975 and 1994; (ii) data on cross-border technological collaborations in the pharmaceutical industry for the period between 1975 and 1995; and (iii) interview data from managers in important positions within the R&D functions from nine pharmaceutical companies (five from Europe and four from the USA) collected in 1997 and 1998.

The US patenting data is used to analyse the percentage of the research effort performed outside the country of origin and the geographical spread of MNCs’ innovative facilities (dimensions 1 and 2 of the globalisation of innovation set out in

section 2). Data on cross-border technological collaborations in the industry is used to examine the growth and geographical distribution of these alliances in the industry (dimension 4). Interview data is used to examine the importance of the international research activities to the overall innovative effort of the pharmaceutical MNCs visited as well as the existence of an international division of labour in R&D and the degree of integration and coordination of these firms' international research effort (dimensions 3 and 5).

4.1 *The percentage of the research effort performed outside the country of origin and the geographical spread of the MNC's innovative facilities.*

The US patenting activity of fifteen of the world's leading US and European pharmaceutical firms was analysed in order to gauge the percentage of the research effort performed outside the country of origin and the geographical spread of innovative facilities. US patents have been used by a number of scholars attempting to measure the extent and nature of the globalisation of innovation (see the work of Patel and Pavitt 1991 and Cantwell 1992, 1995). There are a number of advantages to US patent data for the study of the internationalisation of innovative activities. First of all, patent statistics are available over long periods of time and can be broken down according to firm, technical field and geographical location. Secondly, patent data give information on the country of residence of the inventor which allows the identification of where the research was performed. There are, however, also some disadvantages to these data, above all the fact that in some technological fields patenting can be technically difficult and/or ineffective as a form of protection against imitation. As a result, the propensity to patent varies greatly across technological

areas and industries. However, in the case of pharmaceuticals it is generally recognised that (at least until recently) patenting has been a relatively effective and very important method of intellectual property protection².

Despite the importance of patenting for the pharmaceutical industry, there are still considerable variations in the propensity to patent between different companies and countries. Firms also differ in their propensity to patent in each national market. This may vary according to the costs of patenting fees, the degree of protection awarded by the patent, the size of the market and firms' expectation for exploiting inventions commercially (Patel and Pavitt 1991, Archibugi 1992). Countries also differ in their criteria and procedures for granting patents. Another difficulty with these data is that, in general, national patent offices are biased towards their domestic activity.

According to a number of scholars who have used patent data in their efforts to measure the internationalisation and globalisation of innovation (Patel and Pavitt 1991, Patel 1995; Cantwell 1992, 1995), the existence of differences in patenting behaviour between countries can be partially overcome with the use of US patent data. This is because the screening procedures of the US patent Office are homogenous and rigorous and because the size of the US market means that there is a strong incentive for firms to register their important patents there.

Another set of difficulties which arise from the use of patent data is that patents are often granted under the names of subsidiaries and divisions that are different from those of their parent companies and are therefore listed separately. A further difficulty arises due to regular changes in the ownership of firms through mergers, acquisitions

² This may change as a result of combinatorial chemistry and high-throughput screening which is allowing firms to break patents at a faster rate than in the past. Some major firms are discussing delaying patenting as a result (James Niedel, personal communication, 2000)

and divestures. In order to analyse changes in the location of research facilities as a result of changes in ownership, patents have to be consolidated under the names of their parent companies at regular interval, until recently this process could only be done manually on the basis of publications such as '*Who Owns Whom*'.

The results of an analysis of the US patenting activities of fifteen of the largest twenty pharmaceutical firms in term of sales in 1995 are discussed below. Five companies from the top twenty were excluded from the analysis; three Japanese companies which were not part of the study as well as Astra AB and Pharmacia & Upjohn because their patenting activity was very low. The data is a subset of the US patent database developed at the Science Policy Research Unit (SPRU), University of Sussex². The SPRU database is in turn sourced from the US Patent & Trademark Office (USPTO) patent data. The SPRU Patent database is a well-established database of patents taken out in the USA by companies world-wide. The database studied includes patenting activity for the period between 1975 and 1994. The ownership fifteen companies in the study was consolidated for the years 1975, 1980, 1985, 1990 and 1995 in order to take into account changes in ownership of research facilities as a result of merger and acquisition activities.

Table 1 lists the top 20 pharmaceutical companies worldwide in terms of prescription sales for 1995 according to the industry trade journal *Scrip*.

Table 1 about here

² The author would like to thank Pari Patel for making the database available.

Table 2 presents US patent data for the period 1990-1994 for the fifteen leading European and US pharmaceutical firms studied.

Table 2 about here

The data show the extent to which this sample of leading pharmaceutical multinationals are locating their research efforts outside their countries of origin, how this has changed over time and the geographical spread of this activity.

- (a) When the fifteen firms studied were grouped according to the percentage of their US patenting activity resulting from research performed outside their countries of origin the following patterns emerged (Table 3): With the exception of SmithKline Beecham, in the case of all the other European firms studied 30% or more of their US patenting activities were the result of research activities performed abroad. In the case of three of these firms (Hoechst, Rhone-Poulenc Rorer and Hoffmann-La Roche) 50% or more of their research effort was located outside the country of origin. In other words by 1990-1994 all the leading European firms studied had internationalised an important proportion of their research efforts. The sample of leading US firms studied, on the other hand, seemed to be divided into two categories: a group of four firms whose US patenting activities from research sites outside the home country represented between 10% and 30% of their total US patents; and

another group of four firms whose total US patenting activities accounted for less than 10% of their total US patents. This indicates that while there is a group of US firms that has moved towards the internationalisation of their research effort, an equally large group has remained totally centralised in the home country.

Table 3 about here

The US patent data also show that amongst the group of US firms that had internationalised part of their research effort, this was at much lower levels than the European firms in the sample. In fact, apart from Pfizer, all other US firms performed less than 20% of their research efforts outside the USA. In the case of the European firms, apart from SmithKline Beecham (with 27% of total US patents performed abroad) and Bayer (with 30% of total US patents performed abroad), all the other leading European firms studied performed well over 30% of their research activities outside their countries of origin. The results, suggest the taxonomy shown in figure 1

Figure 1 about here

(b) The US patent data show the increasing importance of the USA as a location for the research effort of European firms from the mid-1970s (table 4)

Table 4 about here

The data show that in the period 1990-1994, patenting derived from work performed in the USA fluctuated around one-third of the total US patenting activities of the majority of European firms in the sample. In the case of one firm, Hoffman-La Roche, research activities in the USA accounted for 63% of the total US patents of that firm. The data in table 4 also show that by the mid-1990s, in six out of the seven European firms in the sample the research effort located in the USA represented over 60% of the total research effort performed abroad. Apart from the two Swiss firms which had substantial research activities in the US before 1975 and SmithKline Beecham (a UK/US firm), the US effort of the other four European firms experienced important increases in the mid to late 1980s and in the early 1990s. The data indicate therefore that from the mid-1980s all leading European pharmaceutical firms were locating a significant part of their research effort in the USA. Considering the much lower degree of internationalisation of research of the leading US firms in the sample, the data suggest that the USA has become a centre of gravity for the research effort of the pharmaceutical industry.

(c) The US patent data of the 15 US and European pharmaceutical firms studied also show that these firms patent from work carried out in just twelve countries namely: Canada, Germany, the UK, Japan, the US, Switzerland, Belgium, Italy, France, Spain, The Netherlands and Sweden. This result indicates that the innovative activities of the major pharmaceutical firms are not very geographically dispersed.

Table 5 about here

(d) US patent data over the twenty-year period studied also give insights into the changes over time in the patenting activity of leading pharmaceutical firms. Table 5 shows that between 1975 and 1994, out of the fifteen pharmaceutical firms studied, ten had increased the percentage of US patenting activities derived from work performed outside the country of origin; two had seen very little change; and three firms had experienced a decline in the percentage of US patents which originate from research work carried out abroad. Though amongst the companies that had experienced an increase in the percentage of US patents that originated from outside the home country there were important differences in the overall percentage of activities undertaken abroad. Grouping the companies according to whether they were from European or US origin, the following pattern emerges: all European companies experienced an increase in the percentage of their US patenting activities resulting from work performed outside the home country. In the case of the US firms studied, three firms had seen an increase in the percentage of their patenting activities resulting from work undertaken outside the US, three had seen a decrease and two firms had experienced practically no change. This result shows that whilst in the case of European pharmaceutical firms there is a clear trend towards the location of research activity outside the home country in the case of US firms there is no clear trend at all.

The US patenting activities of this group of leading European and US firms shows therefore that by the mid-1990s the European firms studied had internationalised an important part of their research efforts. US MNCs showed much lower degrees of internationalisation of their research activities. Patent data also indicate that the research effort of the MNCs studied was not very geographically dispersed but that by the mid-1990s the USA had become a centre of gravity for the research effort of both European and US pharmaceutical MNCs.

4.2 *Cross-Border Technological Alliances*

Next we consider data on cross-border technological alliances, another dimension of the process of globalisation of innovation. Interest in technological alliances has led to the creation of a number of alliance databases above all in areas such as electronics, semi-conductors, and biotechnology (see Chesnais 1988). One of the most widely used and referenced databases on inter-firm partnerships and co-operative alliances is 'The Co-operative Agreements and Technology Indicators' (CATI) database located at MERIT (Hagedoorn 1994, 1995; Hagedoorn and Schakenraad.1990). The main sources for the information collected in these data banks have been newspaper articles, books and specialised technical journals. There are a number of drawbacks to these data including the fact that in general only those agreements which companies make public are published in the press. Newspaper and journal reports are likely to be incomplete, especially when they go back in time and /or regard firms from countries lying outside the scope of the journal. There is also the possible exclusion of small, low profile firms without well-established names (Hagerdoorn and Schakenraad 1990; Chesnais 1988). Despite these limitations alliance databases can give important

insights into cross-border technological collaboration between firms. For this study, a database on technological alliances in the pharmaceutical industry (including alliances with biotechnology firms) was created using *Scrip*, a twice-weekly industry trade journal. Data were collected for the years 1975, 1980, 1985, 1990 and 1995.

Table 6 and figure 2 show the number national and cross-border technological alliances in the pharmaceutical industry for the years studied.

Table 6 about here

The data show the exponential rise in the total number of technological alliances in the pharmaceutical industry in the period between 1975 and 1995 (see Figure 2). The data also indicate a decline in the number of cross-border technological partnerships as a percentage of total technological alliances from the mid-1980s compared to the mid-1970s and early 1980s. The explanation for this is that the rate of increase of US/US technological partnerships, as part of the generalised increase in technological collaborations, was higher than the rate of growth of cross-border technological partnerships. The data, however, also show an exponential rise in the overall number of cross-border technological alliances in the period between 1975 and 1995.

Figure 2 about here

Table 7 shows the importance of US firms, universities and other scientific and technological institutions in technological partnering activity. Since 1980, well over 50% of cross-border technological alliances have involved a US partner.

Table 7 about here

The data therefore supports the notion that cross-border technological alliances have become an important mode for the internationalisation of innovative activity in the pharmaceutical industry and that inter-firm research networks are a key dimension of the process of globalisation of innovation.

The data also show the importance of US firms and institutions as technological partners in this industry. In interviews with nine leading European and US pharmaceutical firms (see Ramirez 2003) both European and US firms singled out the USA as the main location for their technological alliances. A number of factors had come together to make the USA such an attractive location for pharmaceutical research. All companies interviewed singled out the USA as the location for some of the best leading-edge science and technology relevant for pharmaceutical research. Furthermore, it was not only the quality of the science and technology that was important but also the absolute size of the US science-base in terms of the numbers of universities and above all companies and start-ups involved in research. This meant that even though a number of European countries also had state-of-the-art scientific and technological activities, in terms of critical mass they lagged behind the USA.

A second set of factors is related to the US financial system. Venture capital (which had stimulated the creation of technology start-up companies) and the private commercialisation of the results of scientific research were highlighted as key elements making the USA an attractive investment location for major pharmaceutical firms. This institutional set-up had made it easier for European pharmaceutical firms to tap into US scientific research than was the case in Europe, providing companies with an easier mechanism for the appropriation of important scientific breakthroughs. As in the case of foreign direct investment, technological alliance data show the dominant position of the USA for the world pharmaceutical industry (Table 7).

4.3 *Importance of the research effort located abroad*

The importance of the research effort located abroad is another contested dimension of the process of globalisation of innovation. In this research this aspect of globalisation was examined through interviews with senior research managers from a sample of nine leading European and US pharmaceutical MNCs. The companies interviewed were: GlaxoWellcome (UK), Hoffman-La Roche (Swiss), Rhone-Poulenc Rorer (French), Knoll (German) and Sanofi (French), Merck & Co (USA), Johnson & Johnson (USA), Abbott (USA), and Schering-Plough (USA). GlaxoWellcome and Merck occupied the first and second rank in terms of sale for the year 1995; Hoffman-La Roche and Johnson & Johnson were middle ranking firms; Abbott, Rhone-Poulenc Rorer and Schering-Plough were in the lower ranks of the top twenty. Two smaller European firms (Knoll and Sanofi) which were not part of the top twenty were also interviewed. All research managers interviewed had senior positions in their

companies (three of the interviewees were the research directors of their companies and another three were members of their companies global research executives) and all were participants in discussions on the R&D strategies. Most interviews took place between May 1997 and April 1998.

All but one of the firms interviewed (Abbott laboratories) undertook research activities abroad. All research sites located outside the country of origin discussed in interviews performed basic or early-applied research; none of these facilities were for the adaptation of products to local markets. In this respect all the research sites discussed were part of the main research effort of the firms interviewed. Of the five European firms interviewed, four had substantial research efforts outside their countries of origin in terms of the scientific and strategic importance of those facilities (the exception was Sanofi). Apart from Sanofi, the interviews clearly show the importance of the USA as a location for the research activities of European firms in the last two decades. The significance of the USA for European pharmaceutical companies was further reinforced by the recent announcements that Novartis would move its research headquarters to the USA (The Independent 2002) and that the recently merged GlaxoSmithkline would locate its operational headquarters in that country. Of the four US firms visited, three have research facilities outside the country of origin. However, only in the case of Merck & Co (where the company established a research centre on neuroscience in Cambridge, UK) and Johnson & Johnson did these facilities have importance in terms of the significance of their work to the overall technology strategy of these firms.

4.4 *International Division of Labour*

As discussed in section 2, the existence of an international division of labour in research has been identified by a number of authors as the decisive characteristic of the globalisation as against the internationalisation of innovative activities. This dimension of the process of globalisation by leading pharmaceutical firms was also examined through interviews with senior research managers from a sample of nine leading European and US firms (see section 4.3).

Of the five European firms interviewed, four had established an international division of labour between research centres with different sites specialising in different therapeutic/disease areas. These international centres of disease, or therapeutic, expertise grouped together multidisciplinary teams of scientists, physicians and technologists working on particular projects along with people from commercial functions such as marketing and regulatory affairs dedicated to these specific therapeutic areas. The international research effort of the fifth European firm interviewed, Sanofi, was too small at the time of the interviews for this type of international division of labour.

Table 8 and 9 are examples of the international division of labour in research of Hoffman-La Roche and GlaxoWellcome during the mid-1990s

Table 8 about here

Table 9 about here

Along with the creation of international centres of disease/therapeutic expertise, all five of the European companies studied had centralised a number of their big technologies (such as combinatorial chemistry and high-throughput screening) in specific locations that serve the needs of various research sites. In other words, these centres of technological expertise had been organised so as to provide a service to the disease or therapeutic centres. For example in the case of GlaxoWellcome, approximately 50% of the high throughput screening carried out at the company's facility in Stevenage came from requests from the other European research sites. Other key technologies were co-located with the disease or therapeutic areas but had their own separate structures and their own separate heads.

In the case of the three US firms interviewed with international research centres, only Merck fitted the definition of globalised research with a division of labour between research sites. In the case of Schering-Plough, though there was collaboration between the internationally dispersed research sites the company's international research effort was too small to merit a clear division of labour. In Johnson & Johnson's case the company's two research entities were kept separate with little coordination and no integration of research activities.

The results indicate that the existence of an international division of labour between research sites is partly related to the overall size of the international research effort of companies; that is whether sufficient critical mass in specific therapeutic/disease areas exists. It is the companies with the larger international research efforts that are the

most advanced with respect to the development of an international division of labour. Since, it is mainly the European firms that have developed large international research efforts it is also these firms that display the highest degree of globalisation of innovative capacity.

5. Motivations for the globalisation of innovation

Much of the literature on the internationalisation and globalisation of research activities suggest that the international decentralisation of this activity has been the result of conscious, strategic decision-making. The interviews with this sample of pharmaceutical companies indicate, however, that the international expansion of research had to a large extent occurred in a haphazard manner. In most cases research facilities abroad had been the result of the merger and acquisition activities of firms motivated by broad commercial and political as well as scientific and technological considerations. Over time, however, a number of these facilities had been built up to become important research centres while others (including facilities in the home country) had been run down, sold, or closed down.

Despite the generally haphazard manner of international expansion, both US patent data and interview data show that since the mid-1980s European pharmaceutical MNCs had made major efforts to establish research facilities in the USA. Interviews for this research indicate that even in such a 'science-driven' industry as pharmaceuticals, demand (the size, dynamism and sophistication of national markets) as well as supply factors (the national science and technology base) have motivated interest in the USA as a location for research. In the period between the mid-1980s

and the mid-1990s, three of the five European firms interviewed had either made important acquisitions (Rhone-Poulenc's acquisition of Rorer and Sanofi's acquisition of Sterling Winthrop) or undertaken major Greenfield investments (Glaxo's investment in its Research Triangle Park facility) in order to establish their presence in the US market. These major investments had been primarily motivated by the size and dynamism of the US market at a time of relative stagnation in Europe³. However, in both Rhone-Poulenc's and Glaxo's case they had led to important research facilities in the US for those companies (Sanofi on the other hand sold off Sterling Winthrop's research laboratories). A fourth European firm, Hoffman-La Roche, already had important commercial and research investments in the USA. The interviews with European firms indicated that in order to strengthen their commercial position in the US these firms found it desirable to locate research activities in that country.

The interviews also showed that in the 1990s, except for Sanofi, all the European firms visited had made acquisitions or Greenfield investments (in the case of Knoll) in the USA in order to access leading edge science and technology in that country.

European firms were especially interested in establishing research facilities close to the regional clusters of leading-edge scientific and technological excellence in the Boston/Cambridge and California regions in order to become part of existing formal and informal networks. So for example, in the case of GlaxoWellcome and Hoffman-La Roche, the acquisitions of Affymax and Syntex were motivated by both the need to access the science, technology and product pipeline of the acquired companies and

³ Due to the introduction of cost containment measures in healthcare spending, the rate of growth of world pharmaceutical sales slowed down from an average 15% in the mid-1980s to 7% in the mid to late 1990s. The exception is the USA where despite the 'managed-care revolution' sales have continued to grow. As a result in 1998 US prescription drug sales represented nearly 40% of total world market sales and the US market accounted for an estimated 60% of drug company profits (Pilling 1999)

by the European companies' interest to set up facilities in the West Coast of the USA. In Knoll's case the company was particularly interested in being close to the Boston/Cambridge cluster of technological expertise. In the case of the US firms interviewed, only Merck had invested outside the USA motivated by scientific and technological reasons (namely, neuroscience research in the UK). The interviews indicate, therefore, that in their efforts to access new science and technology via mergers and acquisitions or Greenfield investment, the European firms visited were mainly going to the USA. There seemed to be no equivalent force motivating a flow of investment by US pharmaceutical companies to Europe.

The interview data found that a combination of both demand and supply factors had made the USA the favourite location for research of leading US and European pharmaceutical firms. The main trend suggested by the interviews therefore was of a significant shift of research investment towards the USA. This finding supports the notion that the USA has become the centre of gravity for the research effort of the pharmaceutical industry as indicated by data on the US patenting activities of firms and patterns of cross-border technological collaborations.

6. Conclusion

The data presented in this paper show that since the mid-1980s European pharmaceutical firms have been internationalising their research efforts both via FDI and cross-border technological alliances. The most significant trend however is the shift of an important share of these companies' research efforts to the USA. In the case of pharmaceutical MNCs of US origin, the process of internationalisation of

research activity is far less clear; though some MNCs have established a research presence outside the USA the majority of the research effort has become more consolidated in the home country. With respect to the globalisation of research, the results of this research indicate that it is the large European MNCs with a significant international research presence that are moving towards the establishing of an integrated international division of labour in research. The establishment of international centres of disease/therapeutic expertise and the centralisation of major technologies in specific locations from which they service the needs of geographically dispersed research sites are a clear indication of this process.

Much of the attention of the literature has focused almost exclusively on the importance of developments in science and technology in the USA as the main motivation for the location of research activities in that country. The interview data in this study confirms the significance of the existence of a large critical mass of companies, academic and research institutions performing state-of-the-art scientific and technological work as one of the main forces attracting the location of innovative activities in that country. However, the study also indicates the weight of demand factors- above all the size, dynamisms and sophistication of national markets- in the decisions affecting the location of research facilities. At the same time institutional factors- such as the relative ease with which companies can access and appropriate new science and technology through alliances with academic institutions and new science and technology companies- have made the USA an attractive location for firms from this industry. Therefore, demand, supply and institutional factors have come together to make the USA the present centre of gravity for world pharmaceutical research.

Table 1: Top 20 Pharmaceutical Companies Worldwide in Prescription Sales for the Year 1995.

(Figures are for the year ended December 1995, except for the three Japanese firms whose figures are for the year to March 1996)

| Rank | Company | Pharma sales (US \$ mill) |
|------|-----------------------------|------------------------------|
| 1 | GlaxoWellcome (UK) | 12,586 |
| 2 | Merck (US) | 11,314 |
| 3 | Novartis (CH) | 10,571 |
| 4 | Hoechst Marion Rousel (DE) | 8,438 |
| 5 | Bristol-Myers Squibb (US) | 7,810 |
| 6 | Pfizer (US) | 7,072 |
| 7 | American Home Products (US) | 7,005 |
| 8 | Hoffman-La Roche (CH) | 6,800 |
| 9 | Johnson & Johnson (US) | 6,274 |
| 10 | SmithKline Beecham (UK/US) | 6,088 |
| 11 | Eli Lilly (US) | 5,992 |
| 12 | Abbott (US) | 5,629 |
| 13 | Takeda (JP) | 5,621 |
| 14 | Pharmacia & Upjohn (US/SWE) | 5,235 |
| 15 | Astra (SWE) | 4,936 |
| 16 | Rhone-Poulenc Rorer (FR) | 4,841 |
| 17 | Bayer (DE) | 4,619 |
| 18 | Sankyo (JP) | 4,353 |
| 19 | Schering-Plough (US) | 4,281 |
| 20 | Yamanouchi (JP) | 3,576 |

Source; *Scrip Yearbook* (1997)

Shaded area: companies not included in the study.

Table 2: Summary of the number and percentage of home and foreign patents taken out at the US Patent Office by large European and US pharmaceutical firms

| Companys | Number of patents home country | Number of patents abroad | % of patents home | % of patents abroad | % of patents from US sites |
|---|--------------------------------|--------------------------|-------------------|---------------------|----------------------------|
| GlaxoWellcome (UK)⁴ | | | | | |
| 75-79 | 29 | 1 | 97% | 3% | 3% |
| 80-84 | 52 | 1 | 98% | 2% | 0% |
| 85-89 | 67 | 2 | 97% | 3% | 0% |
| 90-94 | 166 | 99 | 63% | 37% | 31% |
| Novartis (Switzerland)⁵ | | | | | |
| 75-79 | 209 | 77 | 73% | 27% | 36% |
| 80-84 | 195 | 91 | 68% | 32% | 29% |
| 85-89 | 184 | 119 | 61% | 39% | 32% |
| 90-94 | 221 | 183 | 55% | 45% | 31% |
| | | | | | |
| Hoechst Marion Roussel (Germany)⁶ | | | | | |
| 75-79 | 178 | 129 | 58% | 42% | 11% |
| 80-84 | 164 | 166 | 50% | 50% | 14% |
| 85-89 | 208 | 224 | 48% | 52% | 26% |
| 90-94 | 296 | 336 | 47% | 53% | 28% |
| | | | | | |
| Hoffman- LaRoche (Switzerland) | | | | | |
| 75-79 | 47 | 97 | 28% | 72% | 63% |
| 80-84 | 70 | 114 | 38% | 62% | 42% |
| 85-89 | 70 | 167 | 30% | 70% | 55% |
| 90-94 | 71 | 281 | 20% | 80% | 63% |
| | | | | | |
| SmithKline Beechams (UK/USA) | | | | | |
| 75-79 | 87 | 4 | 96% | 4% | 4% |
| 80-84 | 75 | 102 | 42% | 58% | 58% |
| 85-89 | 214 | 29 | 88% | 12% | 7% |
| 90-94 | 158 | 58 | 73% | 27% | 27% |
| | | | | | |
| Rhone Poulenc Rorer (France) | | | | | |
| 75-79 | 32 | 1 | 97% | 3% | 3% |
| 80-84 | 12 | 0 | 100% | 0% | 0% |
| 85-89 | 59 | 15 | 80% | 20% | 9% |
| 90-94 | 49 | 49 | 50% | 50% | 32% |
| | | | | | |
| Bayer (Germany) | | | | | |
| 75-79 | 351 | 33 | 91% | 9% | 3% |
| 80-84 | 306 | 35 | 90% | 10% | 8% |
| 85-89 | 447 | 185 | 71% | 29% | 23% |

⁴ In 2000, GlaxoWellcome merged with SmithKline Beechams

⁵ In 2002, Novartis opened a new research site in the UK to focus on respiratory diseases. In 2002, the company announced the move of its research headquarters to the USA. All the groups' research in Europe, the USA and Japan will be coordinated from its new HQ.

⁶ In 1999 Hoechst Marion Roussel merged with French company Rhone-Poulenc Rorer to form Aventis

| | | | | | |
|---|-----|-----|------|-----|-----|
| 90-94 | 425 | 179 | 70% | 30% | 27% |
| Merck & Co (USA)⁷ | | | | | |
| 75-79 | 286 | 12 | 96% | 4% | |
| 80-84 | 443 | 21 | 95% | 5% | |
| 85-89 | 436 | 48 | 90% | 10% | |
| 90-94 | 574 | 139 | 81% | 19% | |
| Bristol-Myers Squibb (USA) | | | | | |
| 75-79 | 47 | 0 | 100% | 0% | |
| 80-84 | 41 | 0 | 100% | 0% | |
| 85-89 | 290 | 40 | 88% | 12% | |
| 90-94 | 339 | 74 | 82% | 18% | |
| Pfizer (USA)⁸ | | | | | |
| 75-79 | 119 | 30 | 80% | 20% | |
| 80-84 | 153 | 42 | 78% | 22% | |
| 85-89 | 147 | 72 | 67% | 33% | |
| 90-94 | 181 | 63 | 74% | 26% | |
| American Home Products (USA) | | | | | |
| 75-79 | 131 | 63 | 68% | 32% | |
| 80-84 | 59 | 73 | 45% | 55% | |
| 85-89 | 100 | 48 | 68% | 32% | |
| 90-94 | 153 | 33 | 82% | 18% | |
| Johnson & Johnson⁹(USA) | | | | | |
| 75-79 | 50 | 2 | 96% | 4% | |
| 80-84 | 65 | 7 | 90% | 10% | |
| 85-89 | 116 | 9 | 93% | 7% | |
| 90-94 | 80 | 5 | 94% | 6% | |
| Eli Lilly (USA) | | | | | |
| 75-79 | 174 | 28 | 86% | 14% | |
| 80-84 | 229 | 17 | 93% | 7% | |
| 85-89 | 268 | 15 | 95% | 5% | |
| 90-94 | 227 | 19 | 92% | 8% | |
| Abbott (USA)¹⁰ | | | | | |
| 75-79 | 89 | 14 | 86% | 14% | |
| 80-84 | 98 | 3 | 97% | 3% | |
| 85-89 | 81 | 1 | 99% | 1% | |
| 90-94 | 234 | 2 | 99% | 1% | |
| Schering-Plough (USA) | | | | | |
| 75-79 | 78 | 0 | 100% | 0% | |
| 80-84 | 95 | 0 | 100% | 0% | |

⁷ In 1999 Merck acquired a US company specialising in neuroscience research. In 2001, it acquired a US genomics company.

⁸ In 2000 Pfizer acquired US company Warner Lambert. In 2002 Pfizer acquired US/Swedish company Pharmacia Corporation. In 2000 Pharmacia & Upjohn had acquired the pharmaceutical arm of US company, Monsanto.

⁹ In 1999 Johnson & Johnson acquired a US biotechnology company

¹⁰ In 2000 Abbott Acquired Knoll, the pharmaceutical arm of German Chemical firm BASF

| | | | | | |
|-------|-----|---|------|----|--|
| 85-89 | 152 | 0 | 100% | 0% | |
| 90-94 | 139 | 4 | 97% | 3% | |
| | | | | | |

Table 3: Percentage of patents resulting from research outside the country of origin in the period 1990-1994

| Percentage of patents | Company |
|------------------------------|---|
| 0-9 | Johnson & Johnson (US) Eli Lilly (US) Abbott (US) Schering-Plough (US) |
| 10-19 | Merck & Co (US) Bristol-Myers Squibb (US) American Home Products (US) |
| 20-29 | Pfizer (US) SmithKline Beecham (UK/US) |
| 30-39 | GlaxoWellcome (UK) Bayer (DE) |
| 40-49 | Novartis (Swiss) |
| 50-59 | Hoechst (DE) Rhone-Poulenc Rorer (FR) |
| 60-69 | |
| 70-79 | |
| 80-89 | Hoffman La-Roche (Swiss) |

| Table 4: Percentage of Firm's Total Patents from Research Performed in the USA | | | | | | | |
|---|--------------|-----------------|-----------------------|----------------|--------------|----------------------------|---------------------------|
| | Bayer | Novartis | Glaxo Wellcome | Hoechst | Roche | Rhone Poulenc Rorer | SmithKline Beecham |
| 75-79 | 3 | 36 | 3 | 11 | 63 | 3 | 4 |
| 80-84 | 8 | 29 | 0 | 14 | 42 | 0 | 58 |
| 85-90 | 23 | 32 | 0 | 26 | 55 | 9 | 7 |
| 90-94 | 27 | 31 | 31 | 28 | 63 | 32 | 27 |
| Patents in USA as a Percentage of all Foreign Patents | | | | | | | |
| | Bayer | Novartis | Glaxo Wellcome | Hoechst | Roche | Rhone Poulenc Rorer | SmithKline Beecham |
| 75-79 | 33.3 | 67 | 100* | 26 | 87.5 | 100* | |
| 80-84 | 80 | 50 | 0 | 28 | 68 | 0 | |
| 85-90 | 79 | 67 | 0 | 50 | 78.5 | 45 | 58.3 |
| 90-94 | 90 | 69 | 84 | 53 | 79 | 64 | 100 |

(* In the case of both companies the absolute figure here is 1 patent. Neither company had a research effort located in the US, so this figure is not very meaningful)

Table 5: Direction of Change in the Internationalisation of Research Activities by 14 Leading Pharmaceutical Firms According to their US Patenting Activity for the period 1975-1994

| Increased | Little or no change | Decreased |
|--|--------------------------------------|---|
| GlaxoWellcome Novartis Hoechst Hoffman- La Roche Rhone Poulenc Rorer Bayer SmithKline Beecham Merck Bristol Myers Squibb Pfizer | Johnson & Johnson Schering-Plough | American Home Products Eli Lilly Abbott |

Table 6: Total, National and Cross-Border Technological Alliances in the Pharmaceutical Industry for the years 1975, 1980, 1985, 1990 and 1995

| Year | Total number of technological alliances | Total number of technological national alliances | Total number of cross-border technological alliances | Cross-border technological alliances as a proportion of total alliances |
|-------------|--|---|---|--|
| 1975 | 19 | 5 | 14 | 74% |
| 1980 | 35 | 13 | 22 | 63% |
| 1985 | 91 | 45 | 46 | 50% |
| 1990 | 190 | 75 | 115 | 60% |
| 1995 | 454 | 194 | 260 | 57% |

Table 7: Percentage of Alliances Involving a US Firm, University or Scientific Institution between 1975 and 1995

| Year | Percentage of cross-border technological alliances involving a US firm or institution. |
|-------------|---|
| 1975 | 50% |
| 1980 | 60% |
| 1985 | 78% |
| 1990 | 58% |
| 1995 | 76% |

| Table 8: Hoffman-La Roche: Location of company's main research centres | |
|--|---|
| Switzerland | Basel: bacterial infections, cardiovascular, CNS Basle Institute for Immunology: basic research |
| USA | Nutley: inflammation, metabolic diseases, cancer Palo Alto: inflammation, bone disorders, pain, diseases of the peripheral nervous system and of the lower urinary tract |
| Japan | Kamakura: fungal infection |
| UK | Welwyn Garden City: viral infection, inflammation |
| Belgium | Ghent: biological research for Nutley projects |
| Italy | Milan: biological research for Nutley projects |
| Germany | Penzburg: cancer |
| Since 1990 Roche has also held a majority interest in Genentech, the US biotechnology company. | |

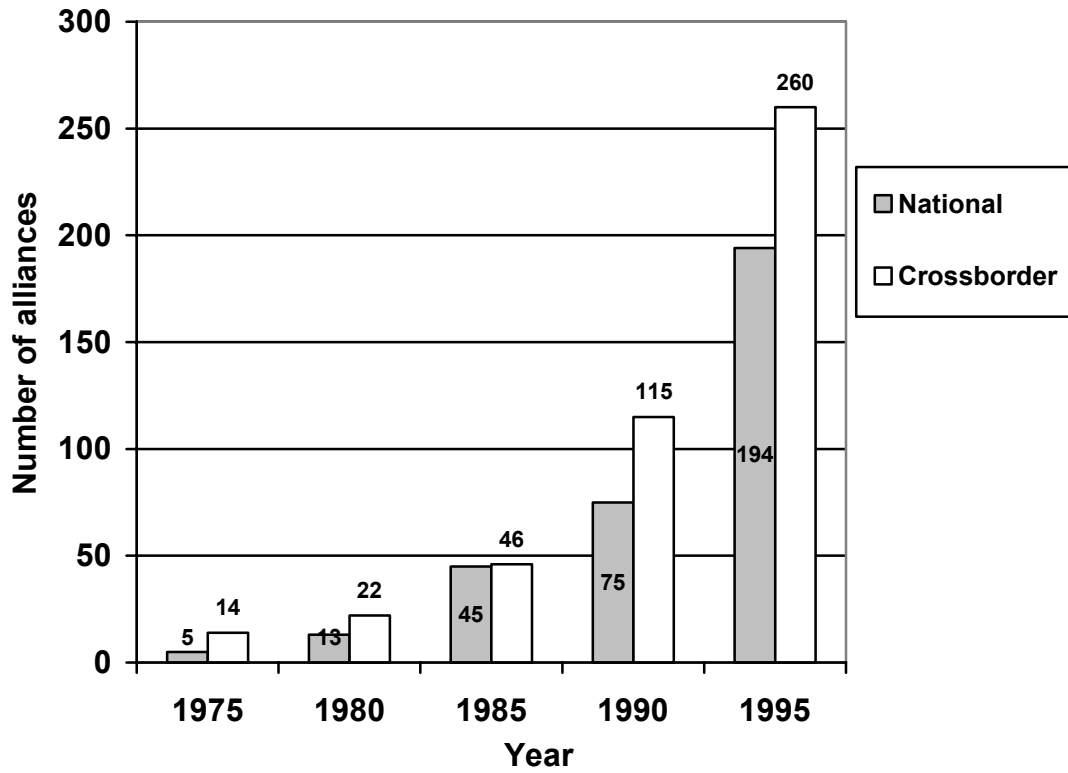
| Table 9: GlaxoWellcome¹¹: Location of company's main research centres | |
|---|--|
| UK | Stevenage: Alzheimers, atherosclerosis, asthma, Tuberculosis, epilepsy, pain. HCV, psoriasis, RA thrombosis |
| USA | Research Triangle Park: cancer, herpes, HPV/HIV/HBV, OA,OP,diabetes, obesity Affymax: combinatorial chemistry |
| Italy | Verona: acute neuronal injury, drug dependency, unipolar depression, novel antibacterials, bacterial pathogenicity |
| France | Les Ulis: ischaemic heart disease, VC risk factors |
| Spain | Tres Cantos: fungal disease |
| Japan | Tsukuba: atopic dermatitis |

¹¹ In 2000, the merger of GlaxoWellcome with SmithKline Beecham led to a major re-organisation of the new company's research organisation. At the time of writing, the company had established six 'Centres of Excellence for Drug Discovery' which brought together groups scientists of different disciplines specialising in a single therapeutic area or collection of diseases. The company had also created three basic research units which brought together the key technologies such as High Throughput Gene Sequencing, High Throughput Chemistry and High Throughput Biology Technologies. The new structure confirms the moved towards the international division of labour identified in the mid-1990s and the increasing importance of the USA as a location for the company's research effort.

Figure 1: Taxonomy of leading pharmaceutical firms in terms of their R&D investment at home and abroad

| | |
|---|--|
| <p>European firms stay in countries of origin</p> <p>None</p> | <p>US firms stay in country of origin</p> <p>Johnson & Johnson Eli Lilly Abbott Schering-Plough</p> |
| <p>European firms go abroad</p> <p>GlaxoWellcome Novartis Hoechst Marion Roussel Hoffman-La Roche SmithKline Beecham Rhone-Poulenc Rorer Bayer</p> | <p>US firms go abroad</p> <p>Merck Bristol-Myers Squibb Pfizer American Home Products</p> |

Figure 2: Number of national and cross-border technological alliances



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