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Multinationals in the Knowledge Economy

- a case study of AstraZeneca in Sweden

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MULTINATIONALS IN THE KNOWLEDGE ECONOMY

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EXECUTIVE SUMMARY

- Multinational companies play a large and growing role in the world economy. They contribute about 10 percent to world GDP and about two thirds to global exports. Their share of global private R&D investments amounts to about 70 percent.

- An important motive underlying the globalization of multinationals' R&D activities is that strategic location of R&D in regions rich in knowledge and technology is a means to augment a firms competitive advantage.

- A critical location factor for pharmaceutical R&D is the host countries' research environment and their capacity to supply a workforce with diversity in knowledge specializations, comprising areas such as medicine, pharmacy, chemistry, biology, informatics and other natural sciences.

- Multinational pharmaceutical companies in small countries depend to a significant extent on knowledge flows and input deliveries from other parts of the world. Because of this, they are strongly influenced by regulations surrounding recruitment of workers' from abroad and employment of foreign experts and researchers.

- AstraZeneca contributes to the Swedish economy through large export sales. The company accounts for about 80 percent of Sweden's total exports of pharmaceuticals and about 5 percent of the country's total exports of manufactures. Moreover, AstraZeneca's net export of manufactures from Sweden is estimated to about 40 billion SEK in 2007. This corresponds to over 30 percent of Swedish total net exports. Sweden's net exports of manufactures were about 120 billion SEK in 2007.

- Analysis of the Swedish units' interaction with the rest of the Swedish economy shows that 'traditional' couplings in the form of transactions with Swedish suppliers are limited. It is instead the company's position in the 'knowledge economy' that makes its presence in Sweden important.

- AstraZeneca accounts for 0.4 percent of the total private employment in Sweden and about 20 percent of the employment of PhDs in R&D.

- In 2006, the R&D investments of Swedish AstraZeneca units amounted to almost 15 percent of the total R&D investments initiated in the Swedish private sector during the same year.

- If one looks at AstraZeneca as a research unit, the company's units in Sweden conduct R&D man-years in the same order of magnitude as the Karolinska Institute and more than the Royal Institute of Technology. Expenditures on collaboration projects with Swedish universities amount to about two thirds of the research budget of a large regional university with about 10 000 students.

- The company's demand for hospitals to participate in different types of projects, such as clinical tests and other knowledge feedback, provides a basis for medical research in Sweden.

- For the triangle Stockholm-Göteborg-Malmö the company can be described as an 'anchor-tenant', i.e. a large firm which demands specialized inputs, in particular knowledge flows and highly educated and skilled workers.

- The challenges and strategic issues faced by pharmaceutical companies imply that the industry will go through structural changes. The strategic choices for pharmaceutical companies comprise a large set of factors. For Sweden, an important consequence is that the companies need to make location choices and build networks that secure accessibility to knowledge, embodied by universities, biotechnology firms and other pharmaceutical firms.

- For the pharmaceutical companies the possibilities to recruit highly qualified personnel is a critical location factor. This is affected by the education systems (including graduate studies), by the conditions for doctors and other employees within the healthcare system to conduct research as well as by the possibilities to recruit personnel from abroad.

CONTENTS

1. INTRODUCTION

Multinational companies play a large and growing role in the world economy. They contribute about 10 percent to world GDP and about two thirds to global exports. In the vast majority of the countries in the world, the presence of multinationals has also been growing over time.

One defining characteristic of multinational companies is that they have high knowledge and technology intensity. For example, they have high ratios of Research and Development (R&D) expenditures relative to sales and a large fraction of their workforce is composed of scientific, technical and other 'white-collar' workers. Estimates show that their share of world-wide private R&D amounts to about 70 percent. Research also demonstrates that multinational companies generate positive spillovers to the countries and regions they are located in. They provide channels for technology and knowledge transfers to domestic economies hosting them. From their dominating role in scientific, vertical and horizontal innovation systems in different parts of the world, they often function as nodes for the diffusion of knowledge and technology. Their linkages to suppliers, other firms, research teams in different research institutions and customers, etc., imply that knowledge and technology 'spills over' to different parts of the economies in which they are located. In view of this, multinational companies play a significant role in the 'knowledge economy'.

This report presents a case study of the role of a large multinational company, active in one of the most R&D and knowledge intensive industries of the world, with establishments in a small open economy. The case study examines the role of AstraZeneca in the Swedish economy, i.e. an economy dominated by multinational companies. They account for almost all of Sweden's aggregate investments in private R&D, over 90 percent of the country's exports and imports as well as a significant share of the total number of employees in the private sector. The analyses in the report make it possible to assess the importance of the local presence of such a large knowledge-intensive multinational for Sweden.

AstraZeneca has three large R&D laboratories in Sweden, located in the country's three metropolitan areas, i.e. Stockholm, Göteborg and Malmö. The head office of AstraZeneca Plc is located in the UK but the head office for early discovery research is located in the Stockholm region. Moreover, the company' major production site for drugs and medicines is also located in the Stockholm region. This production site is one of the largest in the world.

The purpose of the report is to analyze the interaction of AstraZeneca's units in Sweden with the rest of the Swedish economy, and the Swedish innovation system in particular. The following questions are in focus:

- What role does AstraZeneca play for the Swedish economy today and in longer perspectives?

- What role does AstraZeneca play for Sweden as a 'knowledge economy' and what is its importance for the Swedish innovation system?

These questions are assessed from two major perspectives. The first concerns the company's role as an employer in the private sector, its transaction links with other Swedish firms and its role for Sweden's exports. The second perspective focuses on the company's role in the Swedish knowledge economy and innovation system. The report analyses the company as a node for knowledge flows in the Swedish economy and innovation system, and its role as an employer of highly educated and skilled workers in Sweden. For example, the study examines the company's collaboration networks with links to researchers at universities and research institutes, collaborations with other firms as well as its importance for the Swedish labor market for PhDs and other research personnel. As for other global R&D intensive firms in Sweden, knowledge and ideas flow to the country through the company's extensive international networks.

Another purpose of the report is to discuss and analyze what location factors that have been of importance for AstraZeneca's development the last 10-15 years and what factors that will be critical for the company in the future. Which conditions will make it possible for the company to retain and perhaps strengthen its present role in Sweden? The presence of large R&D and knowledge intensive multinational companies in Sweden brings great demands upon Sweden as a host country, in particular in terms of its location conditions and characteristics of its research milieu. The report discusses location factors of the following type: accessibility to highly qualified workers, possibilities for clinical research, collaboration opportunities with universities and other research actors, regulations for inflow of foreign researchers, etc.

The report is organized in the following fashion: Section 2 illustrates the role of multinationals in the global economy and reviews recent research on where multinationals locate their R&D sites and for what reasons. Section 3 presents characteristics of the pharmaceutical industry and discusses strategic issues and challenges that pharmaceutical companies are facing. Section 4 describes AstraZeneca's activities in Sweden and analyses its role for the Swedish economy in terms of export sales, employment, R&D investments and a set of other economic indicators. In Section 5 we analyze the company's interaction with the rest of the Swedish economy. We present an analysis of its transaction linkages to Swedish suppliers and the Swedish labor market for both its production and its R&D activities. We also describe AstraZeneca's couplings to the Swedish labor market. In Section 6 we study the company's importance for the Swedish knowledge economy and its role in the Swedish innovation system. Section 7 discusses the location conditions for pharmaceutical R&D in Sweden, and in Section 8 we conclude and present policy conclusions.

2. MULTINATIONAL COMPANIES IN THE GLOBAL ECONOMY

2.1 Multinationals: characteristics and contribution to the global economy

During the second half of the 20th century multinationals have grown at a rapid rate and are today an important part of the global economic system. According to figures presented in McCann (2008a), which are based on a set of UNCTAD reports, the number of multinational companies in the world have increased from about 7 000 in the beginning of the 1970s to about 78 000 in 2005. Moreover, these multinationals comprise about 780 000 foreign affiliates and it has been estimated that they together employ about 73 million workers, i.e. around 3 percent of the global workforce (McCann 2008a).

Figure 1 shows that the value-added generated by multinational companies in 2006 amounted to almost 5 trillion $ US. This means that multinational companies account for about 10 percent of the total value-added in the world, i.e. world GDP. Compared with the 1980s, the contribution of multinationals to world GDP has almost doubled.

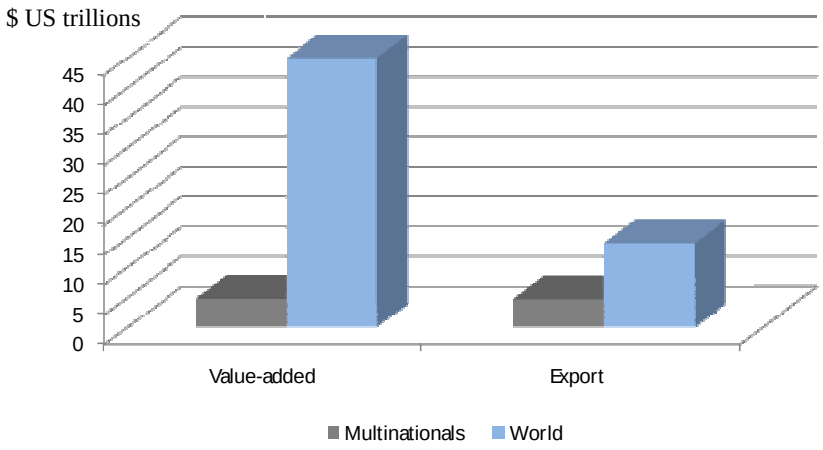

Figure 1. *Contribution of multinational companies to the global economy. Source: McCann (2008a) based on figures presented in UNCTAD (2007) and World Bank (2007).*

Trade flows of multinationals constitute about two thirds of global exports. The value of export flows by multinationals in 2006 amounted to about 4.7 trillion $ US (Figure 1). In recent decades both output, employment and trade of multinationals have grown faster than world trade and the largest component of the global stock of foreign investments is overseas investments by multinational firms (McCann and Mudambi 2004, 2005).

R&D investments are more often than not considered as the driving force in the 'knowledge economy'. Multinational companies are responsible for a significant share of the total R&D investments world-wide. Figure 2 presents estimates of total R&D expenditures by the 700 largest multinationals in the world in terms of R&D as well as figures for global total R&D expenditures.

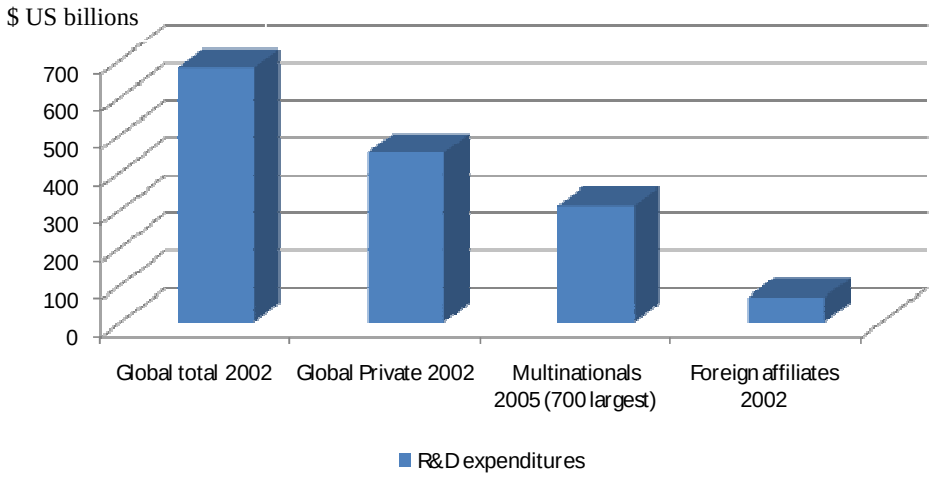

Figure 2.*Contribution of multinational companies to global R&D expenditures. Source: McCann (2008a) based on figures presented in UNCTAD (2005).*

The expenditures on R&D by the largest multinationals is calculated to be about 310 billion $ US in 2005. As a share of global R&D expenditures in 2002 it amounts to over 45 percent and nearly 70 percent of global private R&D. Global private R&D expenditures in 2002 was about 450 billion $ US. McCann (2008a) notes that more than half of the 700 largest multinationals in terms of R&D are active in three sectors: (i) pharmaceuticals and biotechnology, (ii) IT hardware and (iii) automotive. Given the magnitude of these figures, it is clear that multinational companies can be of great

importance for individual economies. McCann (2008b) refers for example to figures showing that over half of China's exports are internal trade within foreign-owned multinational firms and about two-thirds of India's ICT exports are controlled by foreign-owned multinationals.

When it comes to the role of multinationals Sweden is no exception. On the contrary, multinational firms are markedly important for the Swedish economy. Sweden is often characterized as an economy with a strong influence of multinationals in relation to its size. Figure 3 presents the share of (i) employment, (ii) exports of manufactures, (iii) imports of manufactures, (iv) value-added and (v) employees with a long university education (at least three years) for multinational companies in Swedish manufacturing sectors.[1]

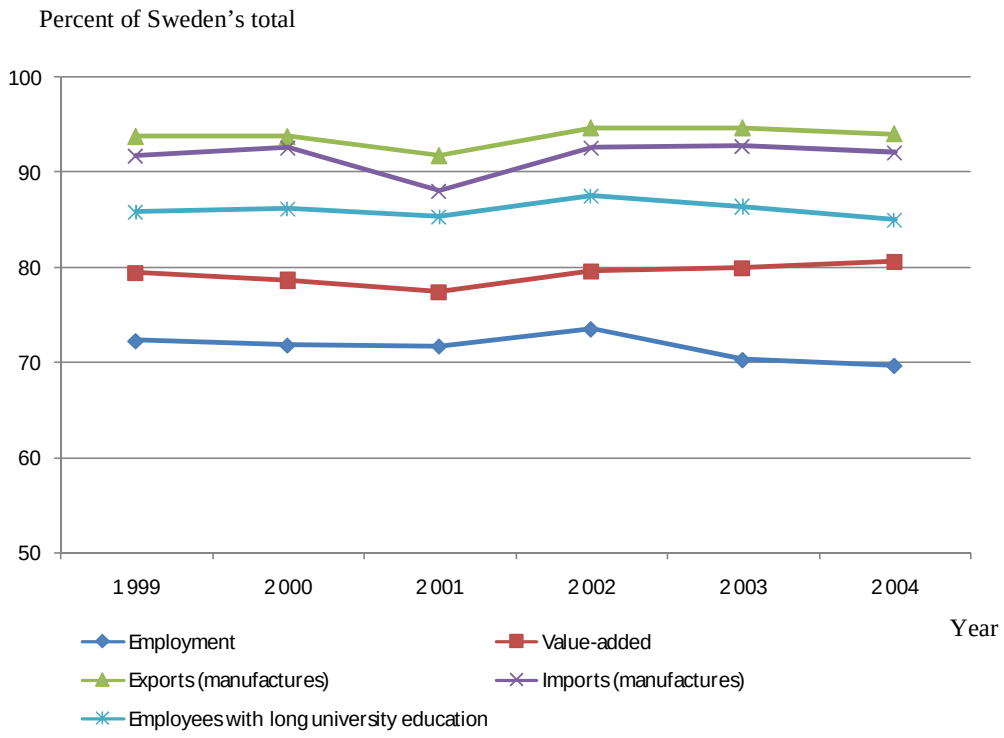

Figure 3. *The contribution by multinational companies to Swedish manufacturing sectors (NACE 15-37) 1999-2004. Source: Statistics Sweden, firm-level statistics*

[1] Figures for multinationals are calculated by summing the values for all firms in manufacturing sectors that belong to a multinational corporation, domestic or foreign. The manufacturing sectors are defined as all sectors between NACE 15-37.

It is evident from the figure that multinationals constitute the lion's share of Swedish manufacturing sectors for all the indicators in the figure. Multinational companies account for over 90 percent of Sweden's total exports and imports of manufactures, and about 80 percent of the total value-added of firms in manufacturing sectors.[2] The corresponding figure for manufacturing employment amount to about 70 percent. The figure also illustrates that multinationals employ persons with higher levels of education than other firms. In 2004, about 85 percent of all workers with a long university education employed by firms in the manufacturing sectors in Sweden were employed by multinational companies. This share is 15 percentage points higher than the share of total employment, which implies that a higher fraction of the employees in multinational firms have long university education. The high knowledge intensity of multinationals is also illustrated by the fact that almost all private business R&D in Sweden (about 95 percent) is performed by multinational firms. Multinational firms are overrepresented in R&D and knowledge-intensive industries (Gustavsson 2004). The research literature shows that multinationals in general have a set of defining characteristics and many of these pertain to their knowledge and technology intensity (see e.g. Markusen 1995, 1998 and 2004):

- They have high ratios of R&D relative to sales
- A large fraction of their workforce is composed of scientific, technical and other 'white-collar' workers
- They have large 'intangible' assets. These assets, defined as the market-value minus the value of tangible assets such as plants and equipment, constitute a large fraction of total market value
- They are often specialized on new and technically complex products
- Multinational companies make large product differentiation efforts, for instance illustrated by large advertising to sales ratios.

[2] See also Johansson and Lööf (2006), and Andersson et al. (2008).

In addition to the fact that multinational firms constitute a significant fraction of trade, value-added, R&D, employment and other economic variables of economies across the world, there is a large literature on 'spillover effects' from activities of multinationals in a country or region. A review of the literature can be found in Blomström and Kokko (1998).[3] One argument is that multinational firms play an important role for technology and knowledge transfers to the countries (or regions) they are located in, and that their local presence have positive effects on the local industry. From their dominating role in scientific, vertical and horizontal innovation systems in different parts of the world, they often function as nodes for the diffusion of knowledge and technology. Their linkages to suppliers, other firms, research teams in different research institutions and customers, etc., imply that knowledge and technology 'spills over' to different parts of the economies they are located in. Using Swedish data, Gustavsson (2004) finds for instance that an increase in the share of employment in multinational companies in an industry leads to an increase in the R&D activities of domestic firms. He maintains that one explanation for these results is precisely that knowledge and technology possessed by multinational firms spill over to the local industry and stimulate their investments in R&D.

In view of the aggregate figures reflecting the role of multinational companies in the global economy as well as in individual economies and the evidence on positive spillover effects associated with their local presence in a country or region, a natural conclusion is that national and regional growth and trade depend to a significant extent on the location decisions of multinational firms (cf. McCann 2008b). It is thus important that individual countries and regions are able to attract and retain activities of multinationals. The documented role of multinationals in the Swedish economy can

[3] There are several other potential effects. Blomström and Kokko (1998, p.2) writes that "local firms may be able to improve their productivity as a result of forward or backward linkages with MNC affiliates, they may imitate MNC technologies, or hire workers trained by MNCs." Other potential mechanisms that they discuss are (i) increased competition that may force local firms to introduce new technology and (ii) spillovers of knowledge and information about foreign markets to local firms, which can make it easier for the latter firms to enter foreign markets. See also Markusen and Trofimenko (2007) who analyze the impact of foreign experts' training of domestic workers on knowledge transfers.

be appreciated in this context. In the next Section we review the literature on the location of R&D activities by multinational companies.

2.2 Location of R&D by multinationals

Modern companies have to formulate business strategies, design organizational structures, and take operational decisions in a global context. Pharmaceutical companies are no exception. Actually, there are few industries so dominated by multinational companies as the pharmaceutical industry (Schweitzer 2007). However, what is typical for this industry is that all its major companies have substantial operations in several countries, and much production as well as R&D activities are performed in countries other than the home country of each corporation.

R&D activities of multinational firms have often been characterized as 'sticky in space' in the sense that their R&D tends take place primarily in their respective home countries (Patel and Pavitt 1995). Indeed, the spatial fragmentation of multinationals' value chains have increased primarily because of changing localization patterns of production activities, in particular routine and less knowledge intensive activities. The globalization of the R&D activities of multinationals is a more recent phenomenon and has developed much slower (cf. Carlsson 2006).

No process has however been immune to the trend of globalization. Since the drive for more rapid and more effective product innovation has been a major factor behind the globalization of companies, it may be perceived as natural that also the R&D function has been strongly affected. Off-shore spending on R&D has increased among the large multinational companies and evidence suggests that the R&D activities of multinationals are increasingly distributed over several concentrations. Multinational companies tend to perform R&D at different locations in the world. It is also documented that over time, R&D activities of multinationals have grown rapidly outside the R&D-intensive 'triad', i.e. Europe, the US and Japan (UNCTAD 2004). Research has also demonstrated that the establishment of internal as well as external R&D networks by multinational companies has become more frequent during the last decades (see e.g. Cantwell 1989, Zander 1999).

The globalization of R&D is interesting, since it has happened in spite of the fact that companies theoretically have many reasons not to globalize their R&D operations. In particular, the spatial dispersion of R&D activities, which implies that R&D laboratories are located in a number of different locations in different countries, generates a number of demanding management problems (De Meyer 1993):

- It is well established that R&D activities are characterized by economies of scale and scope (see e.g. Teece 1987). Successful R&D depends upon a critical mass of scientific and other development competence.[4] Generically, R&D also builds upon the experience of the past, which implies that a dispersion of R&D makes it more troublesome to preserve the historical knowledge base, since much of the knowledge is embedded in people.

- It is a characteristic of R&D activities that they often tend to be abstract and demand a lot of frequent both planned and un-planned direct face-to-face interaction. The costs of direct face-to-face interaction could bring about prohibitive frictions when the interaction has to take place between people localized thousands of kilometers from each other.

- The R&D activities are normally an integrated part of the strategic plans of companies, which they want to keep secret from competitors. It is normally easier to manage secrecy if the R&D activities are geographically concentrated. There is a general tendency among companies to locate R&D in the proximity to their head offices.

- The knowledge generated by the R&D activities is an important intellectual asset of companies. Strategic control of such intellectual assets may be more difficult with a decentralized R&D structure (Steele 1989).

[4] Early studies of multinational R&D emphasized precisely that economies of scale created a drift towards concentrating R&D to the home country, which only in some cases could be outweighed by specific advantages of locating R&D in a "foreign" country (Broström 2008). In this simplified view, an MNE was perceived as determining "the location of its R&D by reconciling centripetal and centrifugal forces" (Hirschey and Caves 1981, cited in Pearce 1999).

- The control of global R&D networks potentially involves several game-like conflicts such as stimulation of creativity versus efficiency and cooperation versus competition between R&D units.

Given the above obstacles, why do companies globalize their R&D activities? And how do they manage their global networks for governance of their R&D activities in off-shore laboratories?

The literature dealing with R&D highlights three major factors behind the globalization of R&D activities and R&D laboratories within companies:[5]

1. *Demand side factors.* Performing R&D activities in other countries can be an instrument to penetrate foreign markets by e.g. developing variants of the current generation of products that are tailored for the customers in strategic markets. R&D located in a foreign market can also be a measure to improve the image of the company in the actual market.

2. *Supply side factors.* The location of R&D to other countries can be a mechanism to take advantage of knowledge spillovers from R&D already performed in that country at universities, research institutes and other companies. Another motivation for locating R&D to another country can be to get access to competencies and skills, which are scarce in the home country or to get access to low cost scientists and engineers.

3. *Competition factors.* The location of R&D in another country can be a strategic reaction to similar location decisions made by competitors or to options neglected by competitors. It can also be an attempt to create a balance between R&D, production, marketing and distribution in a multinational company's value chain.

[5] These general factors apply in principle to all industries. In addition, there are industry-specific characteristics, which govern the decisions to globalize R&D in specific industries. One such specific factor for the pharmaceutical industry is the critical role of the US market for almost all medicines. Since the US market is by far the largest market for drugs in the world, an early approval of a new drug by the Federal Drug Administration (FDA) is critical for securing a rapid growth of sales and profits.

There are several empirical analyses of foreign direct investment (FDI) in R&D. Kummerle (1999) analyzes the propensity of multinational companies to invest in home-base augmenting R&D subsidiaries. He finds that it "rises with the relative commitment to R&D of private and public entities in the target country, as well as with the quality of the human resource pool and with the level of scientific achievement in relevant sciences" (Kummerle 1999, p.18). Also, the propensity to invest in off-shore R&D units to exploit existing firm-specific advantages in foreign markets, depend on the attractiveness of the target country's market. Gassmann and von Zedwitz (1999) report results from almost 200 interviews in 33 multinational companies. The authors identify five trends pertaining to the organization of international R&D in multinationals. These include stronger orientation towards international markets and knowledge centers and establishment of "tightly coordinated listening posts", increased integration of decentralized R&D units and strengthening and reinforcement of foreign R&D sites. Meyer-Krahmer and Reger (1999) present results from 120 interviews in 21 multinational companies. The authors find that the internationalization of R&D is still characterized by "Triadization", i.e. located in the EU, the US and Japan. As regards choice of location, the paper finds an increasingly selective focus on few locations and a concentration of innovation activities to worldwide centres of excellence. The motives for establishing R&D units abroad are maintained to be driven by learning from technological excellence, lead markets as well as interactions between R&D, marketing and advanced manufacturing. Pearce and Papanastassiou (1999) review the literature and indentify two increasingly important roles for overseas R&D in multinational companies. The first motive is to develop new products, or very distinctive variants, for key segments of the global marketplace. Labs with this function are closely associated to other subsidiary functions such as marketing and engineering. Secondly, labs may carry out specialized pieces of basic research that reflect particular areas of expertise within the host-country science-base. Both these roles are confirmed by an analysis of data on UK laboratories. Kumar (2001) conducts an analysis at the country level. This paper finds that US and Japanese MNEs locate R&D in countries with large domestic markets, abundance of low cost R&D manpower and large "national technological efforts". Hegde and Hicks (2005) find that the Science and Engineering (S&E) knowledge base of a nation (as measured by

S&E articles) "critically determines the level and sophistication of US foreign subsidiaries' innovative activity" (p.1). They also find significant differences across industries.

In summary, recent literature put particular emphasis on supply side factors. While rationales related to markets and production certainly matter, knowledge augmenting motives have grown in importance over time (Narula 1999, Narula and Zanfei 2004, Criscuolo et al. 2005). An important motive underlying the globalization of multinationals' R&D activities is that the competitiveness of companies can be improved by having R&D laboratories located in proximity to foreign milieus in which frontier knowledge and technology are produced. Foreign R&D subsidiaries are viewed as important sources of new knowledge and technology (Florida 1997, Braunerhjelm and Svensson 1998, Zanfei 2000) and internationalization of R&D within multinational companies allow them to capitalize on host countries' knowledge and technology (Cantwell 1995, Le Bas and Sierra 2002). Strategic location of R&D in regions rich in knowledge and technology can hence be viewed as a means to augment a firms competitive advantage(s).[6] Kummerle (1997) refers to this type of foreign knowledge and technology accumulation as 'Home Base Augmenting'.

Firms in the pharmaceutical industry are of course highly dependent on R&D. Studies of location of R&D in different industries find that pharmaceuticals is not only an industry in which R&D is highly internationalized, but also a product area where multinational pharmaceutical companies have a particularly high tendency of locating foreign R&D laboratories close to knowledge and technology sources (e.g. von Zedtwitz and Gassmann 2002, Gerybadze and Reger 1999).

For a global R&D network of a company group to function, the internal R&D communication network is of critical importance for the diffusion, validation, integration and adoption of newly created and newly acquired knowledge. An essential feature of communication in an international context is the extra difficulties

[6] Cantwell and Piscitello (2005) maintain that this strategy is distinct from the internationalization strategies in the early post-war period. According to the authors, the internationalization strategy of firms was in this period based on the view that foreign markets should be entered by adjusting product attributes to local consumer preferences, i.e. demand side factors.

caused by geographical distances and cultural differences. The associated frictions relate to a core communication phenomenon in R&D – the informal personal contact (Allen 1977). Over time, the geographical distances *per se* seem to gradually have become a smaller problem due to the improvements in international air connections and in particular, the emergence of the Internet, which has made it possible to create internal electronic information systems for companies. Concerning the cultural distances it has been claimed that they are fairly small within the pharmaceutical industry due to the scientific character of the knowledge base and the "standardization" of the innovation process, which implies that distance in space causes less friction in this industry than in many other industries (Ramirez and Tylecote 2004). On other hand, the high R&D intensity of the industry points in the opposite direction.

When R&D is performed in a global R&D network, networking, i.e. exchange of knowledge in R&D networks, becomes a core element for optimizing organizational learning. When analyzing networks in communication terms, there are four aspects which must be kept in mind: i) the roles of the nodes, ii) the density and the type of communication on the links, iii) the ties to other internal and external networks, and iv) the dynamics of node roles and link density. For a global R&D network to function, each node must have a clearly and dynamically defined vision, which is well known and accepted within the network. Another important aspect is each node's local external network.[7] The local external network is the main mechanism through which each node can extract externally generated knowledge, be it from universities, R&D institutes or other companies. The density, quality and frequency of communication with other local actors are a measure of each node's effectiveness to tap and absorb knowledge in the local network. However, the knowledge acquired locally must be diffused within the corporation's internal R&D network. The local external networks become important first when they are integrated in a strong intra-corporation R&D network.

[7] From a global perspective, local can imply regional as well as national for a small country like Sweden.

3. CHARACTERISTICS OF THE PHARMACEUTICAL INDUSTRY

3.1 Evolution and structure

The contemporary pharmaceutical industry is often perceived as the very symbol of the modern knowledge economy, with its base in science and R&D investments. But the industry's history is young. During the hundred years preceding 1945, drug development was a rare event. The trigger was large scale development of penicillin during World War II. After the war the industry was reshaped and developed formalized in-house R&D programmes, which resulted in rapid rates of new drugs that were introduced into the market. In this phase German companies played an important role.

The take off period between 1945 and 1970 has been characterized as a period when the pharmaceutical firms followed a strategy of random screening, emphasizing that efforts to find new drugs were intensive but not focused. During this period the public sector introduced support to health related research.

The strategic re-orientation after 1970 is a transition towards guided drug discovery efforts, with research methods based on advances in molecular biochemistry, pharmacology and enzymology. In this epoch search is systematic and directed towards design perspectives. Moreover, at this point in time public support for health oriented research becomes established, providing support to a dramatic expansion of R&D and a sequence of profitable innovations. Large firms in the US, UK and Switzerland take a lead in guided drug discovery.

The third phase of pharmaceutical discovery research is quite recent and refers primarily to the period after 1990. The new element is genetic engineering in the discovery and production of new drugs. Molecular genetics and genetic engineering opened up two strands. One employed genetic engineering as a process technology to manufacture proteins, for which the therapeutic properties were already well known.

The other strand used advances in molecular biology to enhance the discovery of synthetic chemical drugs, based on small molecules. In the US this period gave rise to the emergence of a biotechnology startup process, often in the form of university spin-offs.

In the 2000s we can observe a change in the organization of pharmaceutical R&D. Networks for collaboration between different actors become a rule, with the coordination of interactive R&D activities as a decisive activity. In this way pharmaceutical firms can overcome their lack of technical expertise in the realm of genetic engineering, while making use of their downstream capabilities needed for commercialization. The latter includes knowledge about diagnostic tests, procedures for product approval and other aspects of market introduction.

The pharmaceutical industry is dominated by multinational companies. The largest firms are based in a small number of countries, mainly the US, the UK, Japan, France, Germany and Switzerland. All major companies have substantial operations in several countries. R&D activities still tend to be concentrated to a few countries, whereas sales and marketing units are spread world-wide. The industry is founded on its research and development (R&D) and almost all new drugs that reach the market are the result of private R&D (Schweitzer 2007). The individual pharmaceutical companies base their competitiveness, in particular, on their capability to produce new inventions that are patentable and can generate new medicines and drugs (Yeoh and Roth, 1999). Long run success requires a steady stream of new medicines and drugs, of which some must generate substantial profits when they are marketed to cover the high R&D costs. This implies that the pharmaceutical industry is an industry characterized by a high degree of novelty compared to other industries (Ramirez and Tylecote 2004). Another defining characteristic is that a high share of the profits is ploughed back in the R&D process.

Only a small fraction of the new molecules that are developed will ever reach the market and according to estimations done by Harvard economist Frederic Scherer, 55 % of the profits in the pharmaceutical industry come from 10 % of the drugs (Scherer 1993). As an illustration, Figure 4 presents the present value per NCE (New Chemical

Entity) in million US $ across deciles and is based on research by Gabrowski and Vernon (1990). The figure shows that the distribution is highly skewed and only a small fraction of all NCEs can be expected to be able to cover the R&D costs. Pharmaceutical firms thus operate under high risks and need a broad portfolio of potential drugs at different development stages to balance these risks.

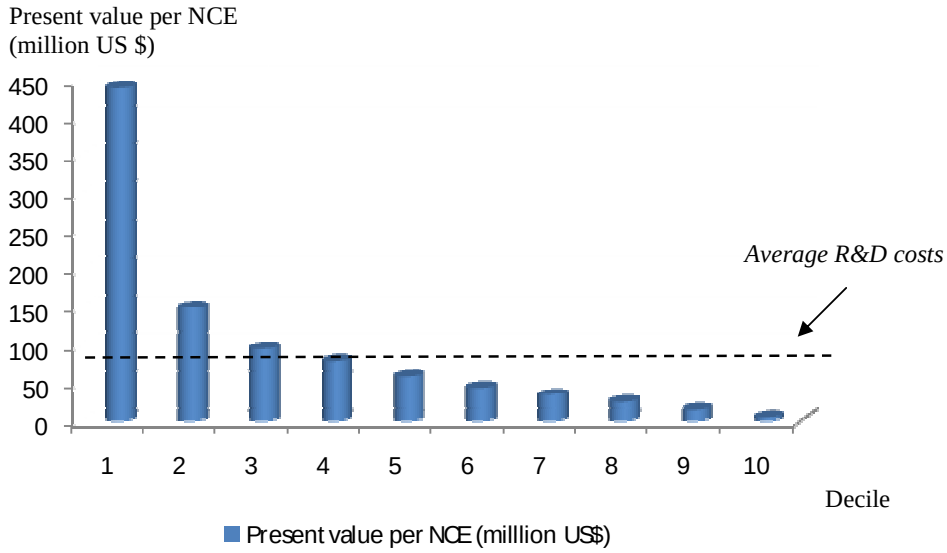

Figure 4. *Distribution of quasi-rents generated by New Chemical Entities (NCEs) in the US market, 1970s (as illustrated in Scherer (1999) based on Gabrowski and Vernon (1990)).*

For a molecule to qualify as a drug it must go through a long test period, which is very resource consuming. There are few or perhaps no other industries which have so long and costly development times as the pharmaceutical industry. Time spans as long as 10-15 years are not unusual.

The long development periods create a special problem for pharmaceutical companies. It widens the gap between the costs generated by the R&D process and the pay-off in terms of incomes from new successful drugs. This implies that the companies have to take decisions on expenditures in different therapeutic areas long before the potential product, if successful, reaches the market. Thus, companies must make advanced predictions with respect to the likely growth rates of different disease

areas, the future state-of-the-art in terms of treatment for different types of diseases, the policies of governments and insurance companies on the spending on and subsidies to different types of drugs, the behavior of competitors and the probability that they will launch new products in the target areas, the state of the general economy, etc. All this adds up to a high level of commercial uncertainty. As a potential new drug goes through the development process, the costs involved increase substantially. It is now a common policy in the industry to kill uncertain projects as early as possible (Ramirez and Tylecote 2004).

One reason why the R&D process is costly is that it is run under a cautious regulatory regime, which demands substantive testing and which covers everything from scientific and ethical regulation to documentation.[8] The documentation is necessary for the development of applications with credible information for the approval of new medicines by the regulatory agencies in different countries.[9]

The high development costs for new medicines imply that a capacity to carry through rapid, low-cost and reliable clinical studies within the regulatory framework for such tests is a major organizational asset and an important source of competitiveness in the pharmaceutical industry (Roberts 1999, Yeoh and Roth 1999).

The profitability of the companies in the pharmaceutical industry is strongly related to their ability to innovate (Roberts 1999), i.e. to the ability to launch enough new products in a timely fashion (Pisano 1997). Of the drugs that are approved and thus reach the market only few generate a financial return, that covers all the related R&D costs, even though the patent protection allows the firms to claim high premium prices for new drugs (Schweitzer 2007). To protect the innovation process in the pharmaceutical industry, patent protection is used extensively and deliberately to create barriers for competitors to enter. Patents are very effective and important instruments of intellectual property protection in the pharmaceutical industry (Ramirez and

[8] Koretz and Lee (1998) provide an example of a new drug, which was tested on 11000 patients in 700 treatment centers in 27 countries.

[9] For almost all medicines and drugs, the US market plays a critical role. Early approval of a new drug by the Federal Drug Administration (FDA) is critical for securing a rapid growth of sales and profits.

Tylecote 2004). Patent protection is critical for the pharmaceutical industry due to its special cost structure with very high R&D costs, but often rather modest production costs. However, when the patent protection expires, the drugs can be copied and sold as generics at a fraction of their earlier price, which implies that earnings will drop sharply.

Even if each specific drug is protected for an extended period by its patent, there is still substantial competition from other drugs addressing the same condition. Many pharmaceutical markets are quite competitive, with strong pressures on companies to diversify and to have a substantial number of drugs at the development stage. Thus, competition is one major factor behind the large number of mergers and acquisitions in the pharmaceutical industry in recent decades. A large number of products at the development stage make it less problematic when some drugs fail during the clinical tests and diversity safeguards companies from loss of market shares if some of its important sources of revenue are lost in the competition.

However, at an overall level the degree of competition is decreasing in the pharmaceutical industry due to on the one hand mergers and acquisitions and on the other an increased concentration of top-selling drugs among fewer and fewer companies (Schweitzer 2007). The degree of competition becomes modified if the level of analysis is changed to consider specific drugs, which actually compete with each other. Thus, the degree of competition is dependent upon how the market is defined. In more specific market segments, the number of competing products can be quite low.

The pharmaceutical industry has gone through a number of fundamental changes in recent decades. The change process has been described as one of progressive vertical disintegration and growing complexity (Gambardella 1995, Cockburn et al. 1999). The original post-war organization of the pharmaceutical sector can be described as consisting of up-stream not-for-profit institutions engaged in curiosity-driven basic research and down-stream for-profit large-scale integrated companies engaged in market-driven applied research.

In the last three decades, the structure of the pharmaceutical sector has become much more complex. The changes of the structure within the pharmaceutical industry have been driven by different factors such as i) the emergence and introduction of new technologies, e.g. information and communication technologies (ICT) and biotechnology, ii) changes in the patent laws to also cover molecular biology and life sciences, iii) the increasing costs for developing new drugs, and iv) changes in demand conditions. These changes have forced firms to enter new therapeutic areas and new markets and to adopt new selling methods (Ramirez and Tylecote 2004, Cockburn 2006).

One important change is the large number of mergers and acquisitions in the industry. The changed ownership structure has been motivated by a need to reduce risks, to renew product pipelines, to access new knowledge bases and technologies, to achieve R&D synergies, to meet the increasing pressure to contain health care expenditures, to broaden markets and to reduce distribution costs (Walsh and Lodorfos 2002, James 2002, Randles 2002, Ramirez 2003, Cockburn 2006).

Another important change is the emergence of a large number of small and medium-sized biotechnology pharmaceutical companies, which has become an important force within the pharmaceutical industry (Schweitzer 2007). Even if these new companies are profit-driven, they have much stronger links to the not-for-profit research institutions than the traditional pharmaceutical companies. They can be seen as an interface between academic and commercial research. Scientists from academia have played a significant role in the founding of many of these companies (Zucker, Darby and Brewer 1998).[10] Over time, the biotechnology sector has consolidated via growth, mergers, acquisitions and exits, while much of the R&D activities in the sector has tended to concentrate globally in a limited number of locations (Furman et al. 2005). Actually, one can distinguish two main types of bio-technology companies:

[10] To a high extent, the US has played a leading role in this process. Two factors have been important in this process. Firstly, the passing in the US congress of a number of laws (the Bay-Dole act, the Stevenson-Wydler act, etc.), made the commercialization of publicly funded research possible and which encourage such commercialization (Mowery et al. 2001). Secondly, the existence of a well-functioning venture capital market in the US and a stock market interested in investing in bio-technology IPOs (Initial Public Offerings).

- "product" companies, acting as horizontal competitors to traditional pharmaceutical companies, and using their knowledge about new techniques and molecular biology to develop and sell their products to the end users in the market, and

- "tool" companies, which live on selling or licensing their leading-edge knowledge or research tools to other companies in the pharmaceutical industry.

The emergence of the new biotechnology companies has generated changes in the relationship between the pharmaceutical industry and universities and this has led to new types of partnerships. A substantial share of the sales of the large pharmaceutical companies now comes from drugs derived from the bio-technology sector (Cockburn 2006).

3.2 Challenges and strategic issues for pharmaceutical firms

The panorama of the pharmaceutical industry's history, contemporary and future characteristics described in the previous sub section informs us that currently the industry faces a series of challenges. First of all, the demands on the industry are growing, and the uncertainty is considerable. The industry signals that it perceives pressures which originate from different sources. For example, there are complaints about the R&D productivity, while at the same time R&D costs are rising. Moreover, the structural conditions for the industry's modus operandi are changing. The challenges associated with the future of the industry can be illustrated by the following set of observations (Gassmann et al. 2008):

- During the past ten years, R&D costs have risen sharply, driven by comprehensive and more complex studies and expensive technologies. These conditions generate a productivity gap in the pharmaceutical industry, where the growing costs combine with a reduced rate at which new medicines and therapies are introduced on a market with stagnating growth (Gassmann et al. 2008).

- Development costs of a new drug are estimated to have grown from around 54 million $ US in the end of the 1970s to over 800 million $ US in the beginning of the 2000s, with additional increases in costs subsequently (DiMasi et.al 2003).

- Prolonged time periods for clinical studies and more complicated administrative procedures reduce the time span during which the patented products remain for profitable sale. During the past four decades, the time to complete clinical studies has increased from approximately 3 years to almost 7 years (Pharmaceutical Research and Manufactures of America).

- High expectations about the return to R&D investments introduce a stress situation in the R&D process, and these expectations are fuelled by historical experiences among investors, who have got used to markets growing at rates around 10 percent annually.

- Each individual research project is characterized by great uncertainties, reflected by an extremely skewed distribution of the returns from projects. The established distribution is such that the 10 percent most successful projects generate more than half of each company's revenues. Only one out of five thousand to ten thousand substances tested make its way to the consumer. Only 3 out of 10 drugs that reach the market earn enough money to cover the average development costs of a new drug (Gabrowski et.al. 2002).

- The market conditions of new drugs are changing due to the increasing efforts put into health economic assessments, which are used as support to the customers' decisions about adopting the drug and associated therapies as a recommended treatment. The same type of studies are also becoming a component of the producers' marketing activities.

- The expectations of patients have gradually evolved from a perspective in which a drug was perceived as a method do tackle symptoms to a view where treatments are expected to maintain a good health quality during the individual's entire life.

This long list of new phenomena in the environment of pharmaceutical firms can be appreciated as an extract of the international research contribution in the last decade. The collected observations inform us that the industry is likely to have to carry out great structural changes, where individual firms have to contemplate adjustments of their strategic behavior. For the industry's large and multinational companies, the strategic choices concern a wide set of decisive factors. In this report, we consider especially the following decision areas:

- Pharmaceutical companies have to reconsider their location choices, while at the same time developing new networks that can ascertain each company's accessibility to knowledge residing in universities, biotechnology firms, and other pharmaceutical firms.

- Accessibility decisions have to consider the combination of local, proximity-based interaction and collaboration that takes place with actors located at large distances. Such considerations comprise interplay in local and global networks and strategic alliances or partnerships, for which agreements are made with regard to each individual development project. Thus, accessibility for interaction cannot be established once and for all, but has to be evaluated from a dynamic point of view.

- Competitive knowledge accessibility can be achieved by companies which have located R&D sites in several local milieus, spread across the globe, where collaboration and other forms of interaction evolves in virtual groups for interaction. Co-location decisions have to be balanced against decisions about long-distance cooperation links. An increasing share of outsourcing is likely to provide the firms with options to – in a direct way – build clusters of co-localized firms.

- Some researchers suggest that new fundamental research in areas such as molecular biology, cellular biology and biochemistry will help to shorten the time span for developing new medicines and therapies. To the extent that this is true, it is obvious that existing and new firms have to participate in a race, where all firms attempt to absorb and adopt the new knowledge and master the new techniques foreseen. Evidently, the competitive advantages may be considerable. Such a race for a new paradigm adds to the uncertainties facing individual firms.

- There is also another source from which individual firms can achieve advantages. The advances in genetic research are expected to offer opportunities to design person-specific drugs and treatments, based on each patient's genetic profile. This potential development could be considered as a dramatic shift of the industry, opening up for pharmaceutical companies to be truly multi-product suppliers, and thereby reduce each firm's dependence on a few successful product variants.

- It has also been argued, though with less substantial underpinning, that pharmaceutical firms may contemplate to identify niche markets and focus on such markets as basis for their choice of R&D strategies.

- New technologies and strategic options that become available in the near future, may cause a shift from a focus on disease-oriented treatment of symptoms to medication strategies that enhance and prolong the individual's quality of life.

4. ASTRAZENECA – activities in Sweden and its impact on the Swedish economy

Section 2 described the role of multinational companies in the global economy. It also illustrated the overall importance of these firms for the Swedish economy. This Section presents an overview of AstraZeneca, a large knowledge-intensive multinational company, in the Swedish economy.

AstraZeneca employs close to 12 000 individuals in Sweden. The firm has both R&D and production activities in Sweden, where all major establishments are located in Sweden's three metropolitan areas, Stockholm, Göteborg (Gothenburg) and Malmö. The current location pattern in Sweden is due to several historical circumstances, of which proximity to university R&D in the pertinent areas has been decisive.

Table 1 presents the total number of employees in Sweden by region and activity. The majority of the employees is assigned to establishments in the Stockholm region. In particular, AstraZeneca's production facilities with over 3 800 employees are located in the Stockholm region. The same region hosts about 37 percent of the firm's total R&D employment in Sweden. The largest fraction of the R&D workers is employed at AstraZeneca's R&D facility in the Göteborg region. The implant business, Astra Tech, is also located in Göteborg. The R&D facility in the Malmö region accounts for about 19 percent of the R&D employment.

Table 1. AstraZeneca employment in Swedish establishments (January 2008)

	Total employment	*R&D*	*Production*	*Other*
Stockholm	7 199	1 651	3 829	1 719
Göteborg	2 417	2 005	0	412
Malmö	1 082	853	1	228
Other	1 146	-	-	-
Sum	11 844	4 509	3 830	2 359

AstraZeneca is the largest actor in the Swedish pharmaceutical industry and its role has grown over time. In the end of the 1990s the pharmaceutical industry in Sweden employed about 14 500 persons.[11] Ten years later the industry had grown to comprise about 16 500 employees. During the same period AstraZeneca's share of Sweden's pharmaceutical employment (excl. Astra Tech) expanded from about 50 to over 60 percent. The firm accounts for about ¾ of the total turnover of the Swedish pharmaceutical industry. Today, between 17 and 18 percent of the total employment of AstraZeneca Plc is located in Sweden.

The presence of AstraZeneca activities leaves considerable marks in the aggregate statistics. The total employment of the firm amounts to about 0.4 percent of the total Swedish private employment. The firm's share of Sweden's exports is more than ten times as large.

There are two basic measures of a sector's role for aggregate exports. The first is the sector's share of total exports. The other is its share of the world export market. Sweden's exports of pharmaceuticals have increased substantially during the last 40

[11] The pharmaceutical industry is here defined as NACE 24420, *Manufacturing of Pharmaceuticals.*

years. Figure 5 illustrates the development of Sweden's share of world exports of pharmaceuticals and it shows a steady increase since the beginning of the 1960s.

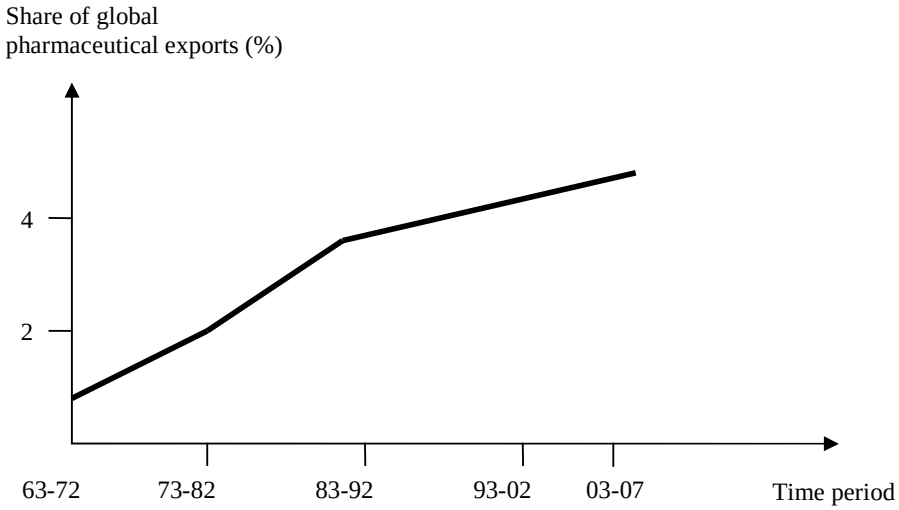

Figure 5. *Sweden's share of global exports of pharmaceuticals 1960-2002 (average share in each period). Source: Statistics Sweden*

In relation to the size of the Swedish economy, Sweden's share of global export flows should fall in the interval 1-2 percent. Paper, pulp and wood products are the largest Swedish export product groups in terms of their share of global exports during the 2000s. All these industries have however experienced a declining export market share for the last 40-50 years. *Other* product groups with relatively large export market share comprise (i) telecom products and (ii) medical products and pharmaceuticals, and these product groups have continued to grow over the long term. During the last century Sweden's share of global exports in each of these two product groups amounts to around 5 percent. This is about twice as large as the corresponding figure for road vehicles.

The strong Swedish position as an exporter of pharmaceuticals reflects that only a few countries develop new drugs and medicines at a larger scale. In this sense Sweden belongs to a small group of countries hosting large-scale pharmaceutical R&D, such as the US, Switzerland and the large countries in the EU.

Comparable data for 2004 show that AstraZeneca accounts for about 80 percent of Sweden's total exports of manufactures by firms in the pharmaceutical industry and about 5 percent of the total exports of manufactures by firms in the manufacturing sector.[12] The total exports of manufactures by firms in the manufacturing sector in Sweden amounted to about 850 billion SEK in 2004. AstraZeneca's share of Sweden's total exports is significant and reflects how the countries' aggregate trade flows are affected by the location of MNEs, in particular for small economies like the Swedish one. In 2007, Sweden's total exports of manufactures (by all types of firms) amounted to about 1 114 billion SEK and the corresponding figure for total exports (including services) was about 1 610 billion SEK.

The majority of the product groups that constitute a large fraction of Sweden's total exports are based on natural resources. It is primarily three knowledge-based export product groups whose share is as large as or larger than pharmaceuticals, i.e. telecom products, road vehicles and machinery equipment.

AstraZeneca's importance for Swedish exports can be put in further perspective by calculating net exports, i.e. the export value minus the import value. In this way one can calculate a net export share:

- Net exports = exports – imports

- Net export share = $\frac{\text{Net exports}}{\text{Exports} + \text{Imports}}$

The net exports of the whole pharmaceutical sector in Sweden amounted in 1997 to about 15 billion SEK. A decade later this figure has more than doubled. The lion's share of this development can be attributed to AstraZeneca:

[12] The manufacturing sector is defined as NACE 15-37. Pharmaceutical exports are defined as the total export of manufactures by firms belonging to NACE 24420, *Manufacturing of Pharmaceuricals*.

- In 1997 AstraZeneca's net exports from Sweden was approximately 8 billion SEK and seven years later this figure had increased to more than 30 billion SEK, that is, more than three times as large. The same figure in 2007 is estimated to be about 10 billion larger. Large net exporters like AstraZeneca provide Sweden with opportunities to be a net importer of other products.

- The net exports of AstraZeneca can be related to Sweden's total net exports. The firm's net export of manufactures is estimated to about 40 billion SEK in 2007. This corresponds to over 30 percent of Swedish total net exports. Sweden's net exports of manufactures were about 120 billion SEK in 2007.

The net export share for the Swedish pharmaceutical industry was about 40 % in 2006 and 2007. The corresponding figure for AstraZeneca is somewhat higher. In this regard one can compare the pharmaceutical industry with the paper, pulp and wood products that are based on natural resources. As a comparison, Table 2 presents total exports and imports in 2007 for three product groups; (i) forest-based products, (ii) engineering industry and (iii) pharmaceuticals.

The large net export share for paper, pulp and wood products can primarily be attributed to domestic supply of forest-based inputs. For pharmaceuticals there is in essence only one fundamental factor of production; the knowledge, the creativity and the experiences of the pharmaceutical labor force in Sweden.

Table 2. Sweden's exports and imports of goods in three large product groups 2007 (Source: Statistics Sweden)*

	Exports (billion SEK)	*Imports (billion SEK)*	*Net export share (%)*
Forest-based	128	32	60
Engineering industry	502	399	11
Pharmaceuticals	59	25	40
Sweden (total for manufactures)	**1 140**	**1 020**	**6**

*) Product groups are defined according to SITC 2: forest-based products (24,25,63,64), engineering industry (71-79), pharmaceuticals (54).

AstraZeneca has an evident importance for Sweden's aggregate exports. It is equally evident that Sweden is of minor importance as a market for AstraZeneca's products. Sweden accounts for a small fraction of the firm's total sales from Sweden. The firm's sales in Sweden and the other Nordic countries constitute about one percent of total sales from Swedish units. The distribution of AstraZeneca's sales from Swedish units is presented in Figure 6.

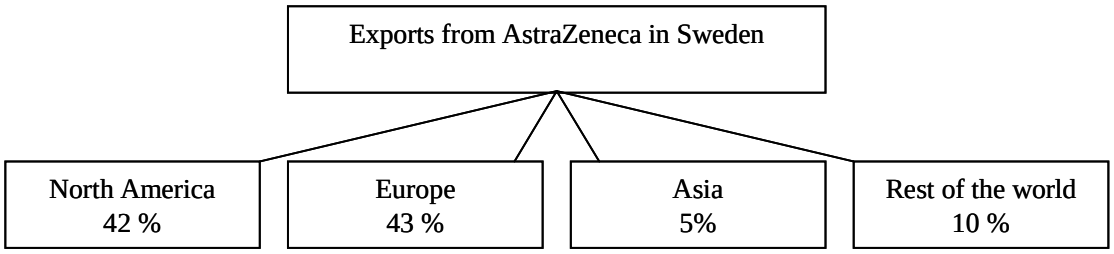

Figure 6. *Distribution of exports from AstraZeneca units in Sweden in 2007. Source: internal figures from AstraZeneca*

The Gross Domestic Product (GDP) measures the aggregate value of all goods and services that are produced in a country during a year. GDP is the most frequently used variable in analyses of countries' growth and development.

Figure 7 shows the value of AstraZeneca's value-added as a share of Sweden's GDP during the period 1997 through 2006. The value-added of a firm measures the value of its production. During 2007 Sweden's GDP exceeded 3 000 billion SEK.

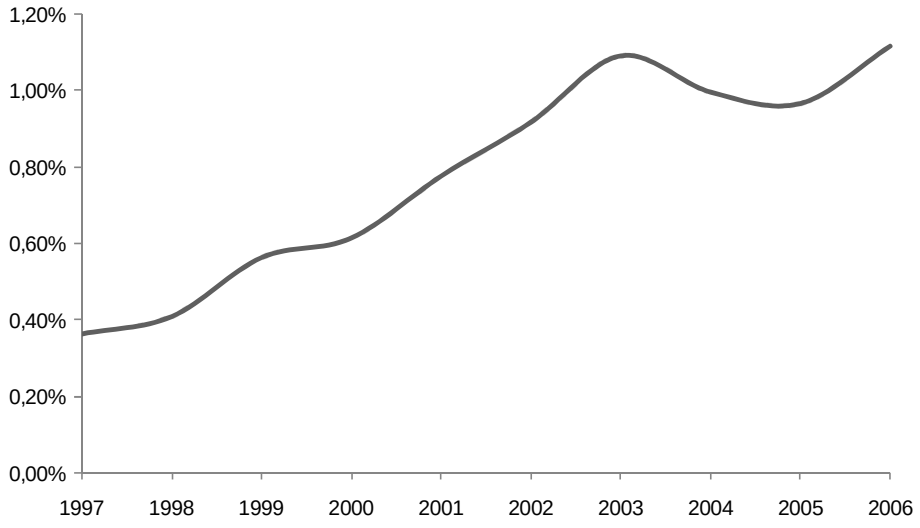

Figure 7. *AstraZeneca's value-added as a share of Sweden's GDP. Source: National Institute of Economic Research and internal figures from AstraZeneca*

The figure shows that AstraZeneca's value-added as a share of Swedish GDP increased from about 0.4 percent in 1997 to about 1 percent in 2006. This implies that the firm's value-added has grown much faster than the Swedish economy as a whole. This development reflects the successful international sales based on drugs such as Losec/Nexium, Seloken and Symbicort and others. The firm's value-added amounted in 2004 to over 26 billion SEK and is estimated to be about 10-15 percent higher in 2006. Its share of Swedish GDP is substantially larger than a typical Swedish manufacturing firm.

AstraZeneca's importance for the Swedish economy can be summarized as follows:

- About 60 % of total employment in the pharmaceutical industry
- 0.4 out of 100 employees in Swedish total private employment
- About 1 percent of Sweden's GDP
- The contribution to Swedish exports of manufactures amounts to about 5 percent
- The contribution to Swedish net exports of manufactures is estimated to over 30 percent.

AstraZeneca in Sweden's knowledge economy – an overview

AstraZeneca's establishments in Sweden form an R&D and knowledge-intensive multinational organization, which demands labor with a diversity of competence profiles. In this role it adds to the formation of the Swedish knowledge economy and contributes to a Swedish research competence of importance for healthcare as well as the life sciences.

R&D is the main activity in AstraZeneca. The firm's establishments in Sweden invested over 12 billion SEK in R&D in each year 2006 and 2007. This figure can be compared with the following figures for Sweden:

- The R&D investments in Swedish firms amounted in 2006 to about 81 billion SEK. The total R&D expenses in universities were about 22 billion.

The R&D investments of Swedish AstraZeneca units in 2006 amount to almost 15 percent of the total R&D investments initiated in the Swedish private sector during the same year. The volume of AstraZeneca's R&D investments initiated by Swedish units can also be illustrated with figures on R&D man-years. Between 7 and 8 out of 100 man-years in R&D in the Swedish private sector can be attributed to AstraZeneca's units in Sweden. The magnitude of these numbers illustrate in itself that AstraZeneca constitutes a major player in Sweden's innovation systems. AstraZeneca's global R&D activities take place in several different innovation milieus and comprise a large

set of collaborations all over the world. Knowledge and information flow within the firm's internal network for knowledge and information exchange. Indirectly these knowledge flows provide the Swedish healthcare system as well as the medical and the pharmaceutical research milieu in Sweden with advantages that other small countries lack.

An important way in which researchers in Sweden can indirectly access the knowledge flows is by means of research collaborations with AstraZeneca. In 2007 AstraZeneca Plc had about 350 larger research collaborations with universities, research institutes and other firms across the globe. Over 20 percent of these are with Swedish actors. One out of three research collaborations in Europe comprise Swedish partners.

Another measure of the magnitude of the R&D activities is R&D outputs in the form of patent applications and granted patents. Patenting is a global phenomenon for most pharmaceutical companies in the sense that they apply for patents in several countries. Between 2000 and 2007 AstraZeneca applied for over 20 000 patents, protection of designs, etc., in different parts of the world. The firm's yearly number of applications to the Swedish Patent and Registration Office (PRV), European Patent Office (EPO) and Patent Cooperation Treaty (PCT) amounted during the same period to about 600. This can be compared with that the total number of applications to PRV is about 3 000.

AstraZeneca's R&D activities in Sweden also generate royalties and incomes from licensing activities. Incomes of this kind from abroad amount to about 10 billion SEK, which corresponds to roughly a fourth of the total export incomes. This form of "knowledge sales" to foreign countries is typical for most R&D-intensive industries in Sweden, but for AstraZeneca they are especially large.

5. INTERACTION WITH THE SWEDISH ECONOMY

5.1 Input delivery networks in production and R&D

Firms play a role in the economy as both suppliers of their output and customers who buy inputs from the market. More specifically, firms interact with the rest of the economy by purchasing inputs from other firms and by delivering goods and services to other firms. These transactions bring about a rather invariant pattern of deliveries, such that the pattern changes at a slow pace between years. The pattern of firms' interaction can be aggregated to a delivery pattern between sectors, forming an intersectoral delivery network. Such a network is recorded in most countries as a Social Accounting Matrix (SAM), in which the deliveries between sectors are a core component, represented by the Input-Output table (I/O table), depicting transaction links between all the sectors of an economy.[13] SAM also includes labor and capital inputs as well as export and import information. SAM can be constructed for regions, countries and entire groups of countries like the EU. In this chapter we employ SAM for the Swedish economy to provide a picture of the role that the company group AstraZeneca plays in the Swedish economy.

With the help of an I/O model it is possible to describe how the expansion of a firm's (and a sector's) output generate additional demand for inputs (goods and services) that the firm uses in its production. In a similar way the model describes how reduced production in a sector impacts the economy by demanding a lower amount of inputs. Such changes have thus repercussions on the activities in other parts of the economy. Expansion generates demand for increased input deliveries, which may originate from domestic or foreign firms. When most deliveries are domestic the feedback from a sector to the domestic economy may be considerable. The feedback becomes weaker as the share of deliveries from foreign suppliers increase.

[13] Transaction links provide an overall image of how different sectors of the economy buy and sell goods and services to and from each other.

As explained above, it matters how large the domestic share of inputs to a firm is. When the share is large the firm stimulates the rest of the domestic economy to a greater extent than when the share of imported inputs is large. In the former case domestic deliverers are stimulated to grow. However, if the domestic deliverers are not capable of offering the right inputs at competitive prices then the firm has to acquire its inputs from other parts of the world. Most large multinational firms are skillful in making use of the diversified specialization that the global economy offers. Obviously, this tendency will be larger for multinationals in a small economy – like the Swedish – than in a larger economy.

The task of the present section is to establish the links or couplings between AstraZeneca and the rest of the Swedish economy with regard to the firm's (i) production activities and (ii) R&D activities. The analysis employs traditional techniques of computing multiplier effects, making use of SAM-information for Sweden and information from AstraZeneca's own accounts. Figure 8 presents the structure of inputs to and outputs from AstraZeneca's production facilities, upon which the calculations are made.

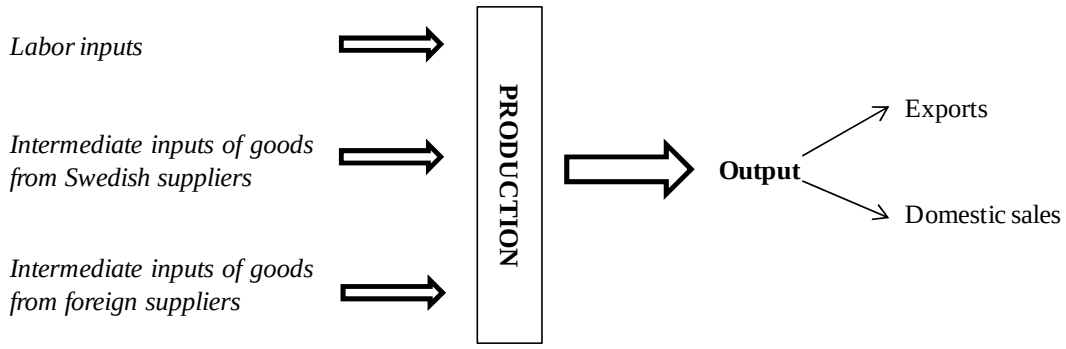

Figure 8. *Inputs to and output from AstraZeneca's production facilities.*

Transaction links between a firm and the set of sectors in the economy are reported in I/O tables also called transaction matrices. An I/O table informs for a sector about the sector's input coefficients, where each coefficient shows the input per unit output, in

value terms, from each of the economy's different sectors. With the help of an I/O table it is possible to calculate the multiplier effects that a sector (or a firm in a sector) has on the total activity in the economy when the output from the sector increases by one percent.

In this section the input coefficients of Astra Zeneca have been estimated for the firm's total production in Sweden and for the firm's total R&D-activities. On this basis the analysis provides answers to two different questions. First, how much is the Swedish economy stimulated when the production activities in Sweden increase? Second, how much is the Swedish economy stimulated when the R&D activities increase? These calculations also provide information about the impact from reduced production and R&D activities.

In order to provide an overall understanding of input deliveries, the inputs of labor, capital and intermediaries are presented as a share of the total costs of AstraZeneca's activities in Sweden. Such an overall picture is presented in Figure 9, where total costs are divided into production costs and sales costs, including marketing and contacts with buyers in different parts of the world. The surplus from production is calculated as sales value minus production and sales costs. This surplus can be used to finance R&D activities.

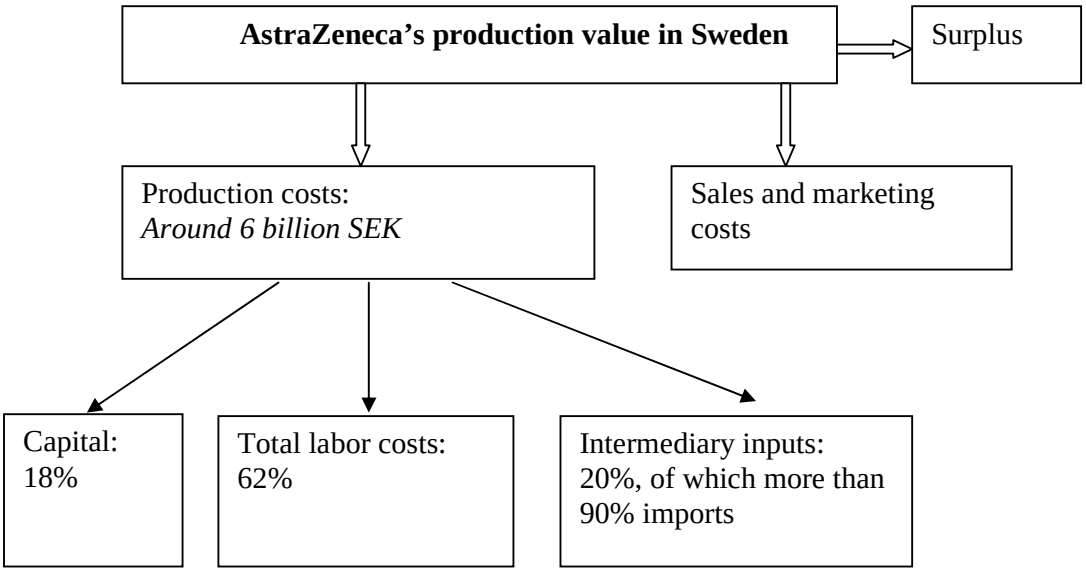

Figure 9. *AstraZeneca's production in Sweden, 2007. Source: internal figures from AstraZeneca*

In AstraZeneca's annual accounts, the costs associated with sales, distribution and administration are reported together, as one compound part. The major share of these costs consists of sales and marketing costs. However, it should be recognized that the sales of AstraZeneca's products are managed by different sales units located in a large number of countries, and the sales operations cover the entire product mix of the company group. The Swedish share of the corresponding costs cannot easily be traced, and the important feature of the costs is that they, in all essence, occur abroad. Thus, sales costs do not stimulate production in other parts of the Swedish economy.

From a technical point of view, AstraZeneca's production value in Sweden is calculated according to the principles for establishing the Swedish national accounts (Statistics Sweden). We may then observe that when the production costs have been determined, we can subtract production costs from the production value to obtain the sum of (i) surplus and (ii) sales costs. If this is done, sales costs have the same order of magnitude as production costs.

The figure shows that costs associated with production amount to about 6 billion SEK. The natural division of these costs is into labor costs (wage sum), capital costs,

and intermediary deliveries. Labor costs comprise the major share of production costs, around 60 percent. Intermediary deliveries correspond to about 20 percent of production costs, and this is a small share, if a comparison is made with the average for the manufacturing industry. The basic observation is, however, that AstraZeneca's production in Sweden is labor intensive. As a consequence, changes in AstraZeneca's production affect other firms in the Swedish economy to a limited degree, since input deliveries from other firms are comparatively small and primarily originate from firms outside Sweden. Stimulation of the Swedish economy is generated via the labor market. These conclusions can be summarized as follows:

- Increased production in AstraZeneca generates very small stimulus to deliverers of inputs.

- Increased production in AstraZeneca stimulates primarily the rest of the economy via increased demand for labor inputs and thereby increased wage sums.

The two observations above indicate that AstraZeneca's Swedish production units have their location because of the available labor force, and that the accessibility to labor inputs outweighs the disadvantage of distant suppliers of intermediaries, including chemical materials. The latter are to a large extent imported, and this accentuates the conclusion about small upstream stimulation of Swedish firms. Rephrasing this into economic jargon, AstraZeneca's production units in Sweden have small multiplier effects on the Swedish economy. As a way to benchmark, the reader may observe that for chemical production in general, an increase in output of one million SEK stimulates the overall economy to grow 2.4 million SEK. This growth stimuli is a consequence of augmented input deliveries and employment increases. In the case of AstraZeneca the corresponding stimulation is not larger than 1.5 million SEK.

In this analysis of AstraZeneca's interaction with the rest of the economy, we have separated the R&D activities from the production activities. There are several reasons for that choice. For R&D activities, the nature of a pharmaceutical company's

upstream and downstream linkages is quite different from the linkages of its production. In particular, since the middle of the 1960s large pharmaceutical companies have gradually allocated an increasing share of their R&D in sites outside the country of the head quarter (Kummerle 1990). Moreover, R&D efforts generate knowledge that is an output in its own right, and the created knowledge represents a property which can be sold or licensed to other firms, and which is often transferred between different units of each individual multinational company group.

Figure 10 presents the costs of R&D activities that are initiated by AstraZeneca in Sweden. The figure shows that more than 40 percent of the R&D investments are carried out with the help of purchases of R&D services, and these services add to the R&D efforts made by AstraZeneca's ca 4 500 R&D workers in Sweden. A major part of the purchased R&D is imported from abroad, and these imported R&D services concern primarily clinical studies which are made on populations in several different countries. Hence, these studies have to be conducted globally.

Currently, the company group AstraZeneca organizes clinical test programmes that involve about 68 000 patients in different parts of the world. Around 3 000 of these patients are Swedish, i.e., about 4 percent. Studies that take place in Sweden have a budget around 120 million SEK, and this budget corresponds to more than 2 percent of the R&D services that are purchased by the company in Sweden.

AstraZeneca's R&D work is labor intensive. About 2/3 of the Swedish in-house R&D expenditures are labor costs, including a crew of consultants who participate in the R&D work. Other components of the in-house R&D costs are capital costs (11 percent) and intermediate inputs (22 percent).

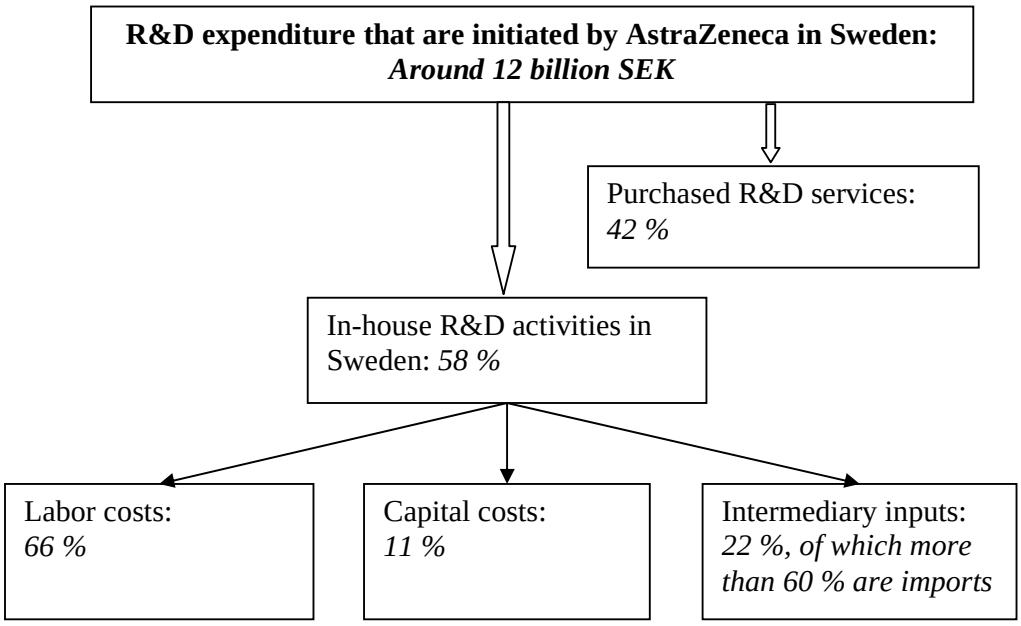

Figure 10. *AstraZeneca's R&D expenditures in Sweden, 2007. Source: internal figures from AstraZeneca*

How important is AstraZeneca's R&D budget in Sweden? As will be discussed later the budget corresponds to around 15 percent of the total R&D spending by private industry in Sweden. However, here we want to discuss how a change in AstraZeneca's R&D investments in Sweden will affect the Swedish economy in the short run via different multiplier effects. With the help of social accounting calculations it is possible to show that an increase of AstraZeneca's Swedish R&D by 1 billion SEK will generate increased input deliveries, and increased employment with growing wage sums that together will make the Swedish economy grow by 750 million SEK. Thus, the overall stimulation is smaller than the increased budget, and this is primarily caused by the large share of imported R&D services. Moreover the inputs used in the R&D work are also to a large extent imported, and this circumstance also lowers the stimulation of the rest of the economy. In a longer time perspective the increased R&D budget can be expected to generate income flows in the form of royalties and license payments.

In summary, the traditional network analysis presented in this subsection demonstrates that AstraZeneca's links to other economic actors in the Swedish economy are thin in a similar way that one often finds for multinational companies in many industries. Like other multinational pharmaceutical companies, AstraZeneca in Sweden has instead well developed international networks – with regard to both its production and R&D activities. The AstraZeneca units in Sweden stimulate the rest of the surrounding economy primarily via the labor market. Growing production and increasing R&D generate expanding income, which stimulates demand in the economy.

5.2 Couplings to the Swedish labor market

In general, large multinational enterprises have an important role in the development of the Swedish labor market, by diversifying the demand for new types of skills and knowledge, and by learning on the job effects as people are employed in the pertinent firms. Of special importance is the international interface that many employees get when working in a multinational firm. Thus, the major influence from Swedish multinationals is their effects on knowledge growth and expansion of international trade.

International research recognizes the long-term impacts from large research-intensive firms and their influence as "anchor-tenants" for other small and medium-sized firms. According to this hypothesis, anchor-tenants support the evolution of knowledge and competencies which would not have developed without the presence of the research-intensive firms in each individual functional urban region. The message is that the anchor-tenants generate qualities to the economic milieu in which they are located, and that these qualities spill-over to other firms in the milieu, including firms that interact more persistently with the anchor firms. An article by Agrawal and Cockburn (2003, p. 1230) expresses this as follows:

> "… large anchor-tenant firms thicken factor markets differently than many small firms that equal the size of the anchor tenant in the aggregate. Economies of scale and scope allow large firms to employ workers with highly specialized skills such as experience in large-scale manufacturing, taking firms publicly and entering foreign markets. The presence of workers with these skills and in local labor markets may make these skills available to smaller firms."

The different AstraZeneca sites in Sweden are themselves anchor-tenants in each of their locations. However, the AstraZeneca's establishments in the Stockholm region (Södertälje) have benefited considerable from a neighboring tenant, namely the Scania establishment in Södertälje. The multinational company Scania has a long tradition in developing *lean-production* techniques, and because of this the local labor market is an excellent fishing area for other companies which demand labor with lean-production experiences. The AstraZeneca management of the production sites in Södertälje recognizes this fact as an important regional milieu characteristic that has favored the company's process innovations over a long period of time.

At the same time, AstraZeneca also functions as an anchor-tenant itself, and it does so in a country-wide sense, with its locations in all three metropolitan regions of Sweden. In this context, the company has in a marked way been a driving force in the development of those knowledge and competence profiles that characterize R&D and production of the pharmaceutical industry. This influence is evident for Sweden's three large functional urban regions Stockholm, Göteborg and Malmö, in which the presence of the company has stimulated university research and the start-up of new firms in the biotechnology area.

It should not be a surprise that AstraZeneca's large R&D activities are knowledge dependent. Less well known is that the firm's manufacturing activities have high knowledge intensity, with a considerable amount of employees with at least three years of university education. Table 3 presents the composition of the labor force, divided into (i) PhDs, (ii) engineers, and (iii) other university educations extending

three years or longer. AstraZeneca's R&D and production operations in Sweden can be described as follows:

- Close to 100 percent of the employees occupied in R&D activities have three years or longer university education, when excluding some basic support activities

- In production, the share of employees with long university education (three years or longer) is about 20 percent. This figure is around four times as large as the average for a typical manufacturing firm.

Tabell 3. Composition of the employment in AstraZeneca's Swedish units

	R&D	***Production***
PhDs	1 070	31
Engineers	495	325
Other employees with long university education	3 040	367
Share of total employment	***100%***	***about 20%***

AstraZeneca's R&D operations in Sweden had in 2007 a staff of more than 1 000 researchers with a PhD education. This figure could be assessed as follows:

- The total number of R&D workers with a PhD in Swedish firms was in 2005 about 5 000

- At the same in time, the medium-sized Jönköping University employed around 150 full time PhDs

- Turning to the Royal Institute of Technology i Stockholm, we find that the number of PhDs amounted to 700, while the number of doctoral students was ca 1 500.

- In year 2005, the number of full time R&D workers at Karolinska Institute was about 1 700.

The above comparisons illustrate that the size of AstraZeneca's R&D efforts can be compared with a technical university like the Royal Institute of Technology (KTH), when the input of PhDs is the benchmark variable. On top of this, AstraZeneca's R&D operations currently employ about 3 500 engineers and other employees with a long university education, comprising at least three years.

At a finer level of specification, which profiles can be found among AstraZeneca's R&D staff? The researchers comprise people with an orientation towards analytical chemistry, pharmacy, molecular and integrated biology, but also physicians, and engineers. In this way the company offers job opportunities and career tracks for individuals with an academic education in a variety of disciplines such as chemistry, biochemistry, microbiology, pharmacology and pharmacy. In addition there is a wide interface with almost all specialties of medicine.

Table 4 reports on the functional division of AstraZeneca's employees. The table shows that a major part of the workforce is occupied with tasks that can be characterized as knowledge handling, signifying labor that elaborates and disseminates information or detects, develops and diffuses knowledge in the internal networks of the firm.

Table 4. Functional composition of persons employed in AstraZeneca's establishments in Sweden (January 2008)

Functional division	*Number of employees*
R&D	4 509
Production	3 830
Corporate management and governance	330
Human Resources and R&D management	228
Information systems and IT	211
Sales and distribution	366
Support functions	1 423
Astra Tech (subsidiary of AstraZeneca PLC)	947
Total	11 844

A conclusion from the preceding discussion is that AstraZeneca imposes demanding requirements on the Swedish supply of knowledge-intensive labor through its R&D activities as wells as its advanced production and logistics activities. The R&D operations generate a demand for a diversity of bio-medicine educations. From the perspective of the Swedish society, AstraZeneca in this way offers career tracks outside the university area for undergraduates and graduates from a wide set of university disciplines. Without these tracks the Swedish universities would not have the opportunity to maintain education programmes at the current level. In a future perspective, the current interplay between the pharmaceutical industry and the university education in Sweden reproduces the knowledge base in areas such as bio chemistry, micro biology, pharmacology and research on "large" molecules, and these are areas with potential applications outside drug design and production.

AstraZeneca is a prime motor in the segments of the Swedish labor market discussed above. In the middle of the 1990s more than half of all persons working in the Swedish pharmaceutical industry had their employment in AstraZeneca. Ten years later this figure had risen to 65 percent. At this time, 17-18 percent of the total labor force of the company group AstraZeneca had their jobs in Sweden.

Being such a large actor in small and specialized segments in the Swedish labor market, how does AstraZeneca manage to recruit its personnel? One aspect that we will return to is that the recruitment options differ between the company's different sites. For R&D workers, the annual turnover can vary between 2-5 percent across the sites. This means that there is a considerable knowledge renewal process from the perspective of the company, while it also implies that knowledge diffuses to other parts of the economy and society.

Studying the recruitment processes in the Swedish pharmaceutical industry in Sweden, it seems reasonable to conclude that the university system manages to produce a matching amount of young researchers across fields that are relevant for the industry. In addition, the recruitment activities can employ well established interaction networks which connect actors who represent demand and supply of university educated labor. However, the recruitment of research leaders and managers is more problematic, because in this case the industry tries to attract persons with a long period of experience. Since AstraZeneca has such a dominant position in Sweden, there are few other domestic firms from which experienced research leaders can be recruited. As a consequence, research leaders are often searched for with the help of headhunting procedures, and the sources for new staff extend over Europe, with UK, Germany, France and Denmark as important search fields.

6. R&D AS A GENERATOR OF WEALTH

6.1 Knowledge and knowledge handling in production and R&D

Pharmaceutical companies are recognized as R&D intensive, and because of this many observers find it natural that they have a much larger share of employees with long and specialized education. Many of the largest international pharmaceutical firms still have a two-pronged structure, with knowledge creation as the prime line and drug production as the second. In the period after 2000 it is possible to identify a development along which knowledge production gradually becomes separated from drug production. The change points in a direction where the drug manufacturing activities are outsourced to separate firms.

AstraZeneca's activities in Sweden 2007 had the classical structure in which R&D and manufacturing are parallel activities. If the manufacturing activities and associated support functions are studied in isolation, we can still observe that also the manufacturing processes are clearly knowledge intensive. This is explained by a whole chain of knowledge-dependent operations such as quality control, where inventories and packages are inspected on a regular basis, and where chemical processes, pharmaceutical agents and final drug products are examined and tested according to scheduled plans. Among others, process engineers, chemists, and dispensers participate in these control routines. Obviously, a large share of the pertinent workforce has a background with 3-5 years of university studies.

The R&D work in a pharmaceutical firm comprises the design of new pharmaceutical products, but also development of already existing drugs and preparations as well as therapeutic procedures and prescription schemes. The latter part of R&D efforts include alternative formulations, strengths, packaging solutions as well as extended use of a drug to new diagnostic indications. It should be observed that a new pharmaceutical product has first to pass a several-year period of pre-clinic research processes, in which a major task is to formulate new molecules with desired and warranted features. Such substances are tested in various ways, including tests on

animals. In this context, there are two issues, where the first is the medicine's effectiveness and the second is its safety.

When the first pre-clinic phase of the drug design process is successful, then it can enter its development phase, which comprises final drug formulation and a series of clinical studies of the drug's effects as well as its side effects. This transition is usually referred to as a shift from a *discovery phase* to a *development phase*. Those drugs that enter the development phase also need patent protection, and the patenting activities are demanding in their own right. Moreover, a product must be approved in each country where it will be marketed, and the approval process also requires special skills and a fair amount of interaction. Finally, when the development work reaches this stage, the company has already manufactured a product stock so that distribution can start immediately after a drug is approved. The sales revenue must come without delay, in view of the fact that many drugs have accumulated R&D costs during a period of 10-15 years, and these costs have to be covered by income flows. In addition, the period of patent protection is limited.

The extremely long period of R&D investments in a particular product and the associated accumulated costs thus provide strong incentives to start the production without unnecessary delays. As a consequence, the process R&D to a large extent has to take place in combination with the ongoing manufacturing activities. In this way, the rationalization and efficiency augmenting R&D efforts in the Södertälje manufacturing establishments become an integral part of the production itself. Improvement groups and quality circles bring about stepwise improvements along the principle of *lean production*, as developed by the Toyota company. The AstraZeneca process R&D in Södertälje is to a large extent inspired by the practices of the Toyota and Scania companies. During the entire life cycle of a pharmaceutical product a lot of attention is given to activities that industrial economists call process R&D, where gradual improvements of routines are carried out in order to reduce production costs. Such efforts are necessary, because the overall pattern for a pharmaceutical product is that its price in most markets falls over time, partly as a result of competition and partly because of price regulations by authorities in many countries. This implies that

for many products it is required that costs can be reduced by as much as 5 percent annually.

The described conditions for drug manufacturing and deliveries have the effect that process R&D becomes a considerable part of the R&D expenditures of a drug producing company. This helps to explain the observation that manufacturing of pharmaceutical products is a knowledge-intensive activity. In addition, sanction to sell a certain pharmaceutical product in a country requires that the production process and the associated quality control procedures are accepted by the relevant authorities of the country. This means that a company like AstraZeneca has to interact (in matters of manufacturing and delivery quality) with authorities across the globe to get sanctions or permits to sell in each individual country. Again, this makes the drug production different from many other types of manufacturing, and it forces the organization to employ the required competencies. The following remarks illuminate the nature of pharmaceutical manufacturing activities:

- Pharmaceutical manufacturing with integrated process R&D is characterized by persistent development activities rather than simple systems routines.

- Since the end of the last century the manufacturing process has changed in a direction, where pharmaceutical firms increase the employment of precision instruments and techniques, information systems, robotics and nano-engineering. This technology development moves production towards enhanced knowledge intensity.

- All relevant changes in production routines must be documented in a systematic way in order to establish certificates in each market where products are sold.

6.2 From molecules to global products

AstraZeneca's product mix comprises dry substances (e. g. tablets and capsules), inhalation medicines and liquid products (e.g. injection liquids). In all these product areas the company is conducting pre-clinic basic research (Discovery), as well as development R&D (Development). In the beginning of 2008 about 2 000 persons were occupied with basic R&D in Mölndal (Göteborg region), Södertälje (Stockholm region), and Lund (Malmö-Copenhagen region). In the same sites around 2 500 person were involved in development activities such as drug formulation and global programmes for clinical tests.

The entire process of drug development is composed of two main activities, which partly overlap each other. The first activity, which is described in Figure 11, aims at discovery or detection of a combination, consisting of (i) a target protein, which affects the evolution of a certain disease or brings about dysfunctional phenomena, and (ii) chemical agents which can be used to influence the target protein. When the pre-clinic research is successful the clinical studies can be initiated.

For a long period, many firms in the pharmaceutical industry have reported that the complete process, including both discovery and development, extend 10-15 years in time. In recent time AstraZeneca has the ambition to reduce this time span down towards 8 years, making use of various advancements in biotechnology. Shortening the R&D process time may be understood as a reaction to dramatically increasing R&D costs of making a drug ready for the market. The total costs of a new drug have been estimated to be close to 10 billion SEK in year 2006 (Gassmann et al. 2008).

The different steps of the pre-clinic R&D process are illustrated in Figure 11. The basic comments are that for each final pharmaceutical product candidate, the pre-clinic phase runs over several years. A major aspect of the process is sorting ideas and eliminate the vast majority of all attempts. In the period 1950-1975 these elimination activities were based on random screening, whereas the approach in later decades has

been guided screening, based on advances in molecular biology (e.g. Malerba and Orsenigo 2006).

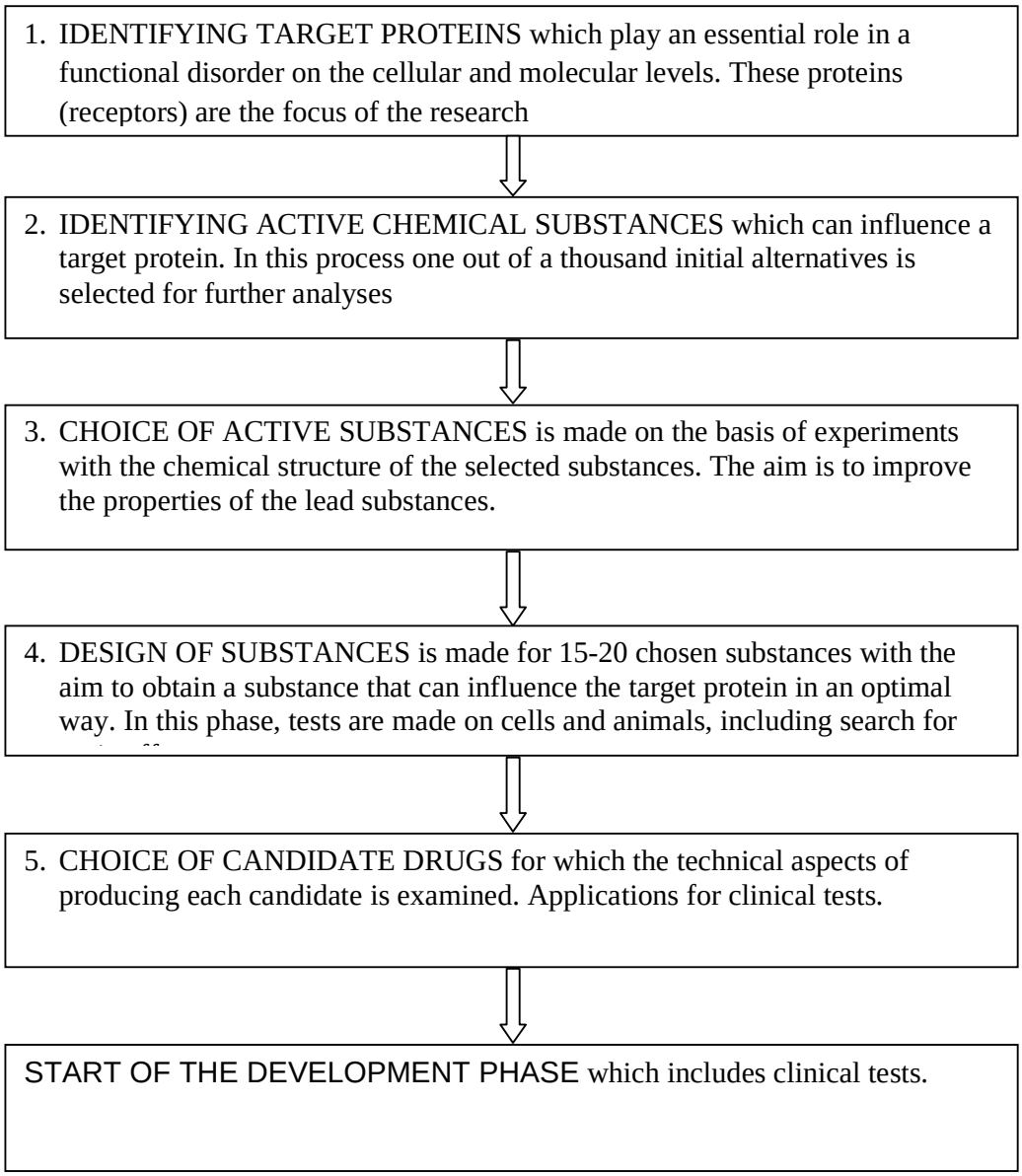

Figure 11. *Illustration of the R&D phases of AstraZeneca's pre-clinic research*

At the time when a candidate substance has been chosen, the development stage starts. In this stage the ambition is to design the drug also from the perspective of its production. The second set of development activities comprises clinical studies, which AstraZeneca describes as four phases of activities:

- *Development phase 1:* The drug is tried on voluntary, healthy test subjects, 50-150 persons.

- *Development phase 2:* The drug is tried on patients with the disease, for which it has been developed. In this phase the number of patients who are treated with the drug is usually 100-200.

- *Development phase 3:* In the third phase, the effects of the new drug are compared with the efficacy of the current standard treatment of the functional disorder or disease. These studies often comprise 5 000 persons or more.

- *Development phase 4:* The new drug or therapy has to be approved and registered in each country, in which it is intended to be used. In this phase new clinical studies are started with the aim to record and analyze the long-term effects of the medicine. Moreover, the medicine's health economic consequences are investigated. These consequences remain an important argument in negotiations about the price of the new medicine.

For those drugs that have been approved for sales, development and control activities continue with a focus on recording and documentation with further proofs of efficacy and additional search for signs of secondary effects. At the same time the company may start to examine the possibilities of trying the drug for other disease indications. An important aspect of these follow-up activities is a systematic investigation of the drug's effects on different age groups and potential differences between male and female patients. A drug's function may also be affected by improvements of the therapy design.

6.3 R&D networks for collaboration with external actors

What determines a company's possibilities to organize successful R&D work? On the one hand, R&D activities require internal resources in the form of knowledge labor and the experiences and knowledge embodied in the firm's R&D workers, as well as

the routines for knowledge creation that the firm has developed over time. On the other hand, the firm can make use of knowledge flows from external knowledge providers. Part of these flows are acquired through purchase, while other parts are the result of cooperation with external researchers, institutes and universities as well as other firms in the same and associated industries. The collaboration with universities has a particular importance. Persons responsible for R&D efforts in AstraZeneca estimate that up to 80 percent of all research related to various forms of cancer are carried out as university research, whilst the remaining 20 percent take place within the pharmaceutical industry.

Leading persons in the industry argue that currently there are so many eminent research milieus across the world that it becomes an impossible objective also for a large pharmaceutical company group to locate in all these environments of knowledge creation. In view of this, a favorable strategy must include the formation R&D networks with links to prominent knowledge producers in relevant fields. AstraZeneca has developed processes and technologies for orchestrating collaboration networks that facilitate knowledge interaction over distance. These links function as an infrastructure for research coordination, knowledge exchange, as well as trade with new research results.

AstraZeneca's global R&D is carried out in a set of R&D units in different parts of the world. Those R&D establishments are interlinked in a network which provides AstraZeneca's production and R&D units in Sweden with qualified knowledge flows from knowledge nodes over the world.

- The AstraZeneca group has organized a scheme for systematic information exchange between the nodes in the group, and this exchange ascertains that specialized information is made available for assessment across the entire internal network of the group.

The Swedish units of AstraZeneca employ collaboration strategies in a far reaching way. First and foremost cooperation takes place between R&D units inside the

company group, AstraZeneca PLC, but the interaction with other pharmaceutical firms has increased over the years. Other external collaborators include universities and hospitals that are in charge of clinical studies.

AstraZeneca's R&D units in Sweden have a large international network for collaboration, but there is also a dense network of interaction links to actors inside the country. This is illustrated in Figure 12. With the help of interviews and other forms of information, it has been possible to estimate that the total number of collaboration and cooperation links amount to about 550, divided in the figure into agreements of collaboration and more well-specified joint research projects. A large share of the collaboration partners are found in Karolinska Institute, Chalmers Institute of Technology, and the universities in Göteborg, Uppsala and Lund.

- Considering the 550 links for collaboration and exchange of knowledge referred to in Figure 12, the estimated branching of direct and indirect contact links represents an area of interface with the Swedish research community in the order of 1 500 persons or more.

- The company's direct and indirect contact links for research interaction can be estimated to comprise 20-25 university research departments in Sweden.

AstraZeneca's collaboration links include various types of cooperation and collaboration such as agreements to carry out joint research, funding of research, sponsoring of students with research grants and other research support, especially in the form of so-called fee for service. Still another form of support is sponsoring of scientific events and meetings.

Figure 12 shows that around 25 percent of the total amount of collaboration links comprise large research projects. In 2006 the resources set off for these 130 major projects is estimated to be 55-60 million SEK. The major part of these R&D expenditures has been classified as pure research cooperation. These figures imply that AstraZeneca supports research and education in Swedish universities and other

research organization to an extent that exceeds the annual costs of a normal university department. To provide a benchmark figure, it is meaningful to observe that a typical research budget at a regional college university in recent years has amounted to around 150 million SEK.

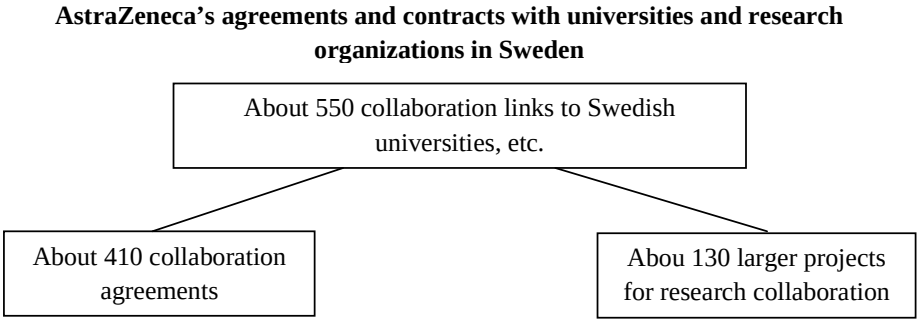

Figure 12. *AstraZeneca's collaboration with external actors in Sweden, 2006.*

From the information presented one may conclude:

- AstraZeneca's financial support to research and education at Swedish universities amounts to about 2/3 of the research volume at a representative regional university. The university in Jönköping with around 10 000 students has had a research volume of ca 150 million SEK.

In addition AstraZeneca works together with Swedish universities by supporting PhD projects, often combined with resources for tutoring and thesis advice allocated to adjunct professors. Moreover, PhDs can get so-called post-doc grants, and many persons who get this type of support are later recruited to take part in AstraZeneca's in-house research. The described forms of resources for young researchers provide support to around 30 persons annually.

6.4 Labor mobility and embodied knowledge flows

The evolution of R&D intensive firms in the pharmaceutical industry is to a large extent determined by two parallel ambitions of each individual firm. On the one hand a firm strives to control knowledge flows in such a way that knowledge does not diffuse – unintended – to competitors. On the other hand the firm will benefit from exchanging information with other actors whenever this will enhance the firm's own R&D processes. These aspects were discussed in the previous sub-section; here we shift the focus to illuminate knowledge flows that depend on labor market mechanisms.

Contributions to the international research literature on knowledge flows emphasize the importance of labor market mobility as an important vehicle in diffusing knowledge both between firms in the same industry and between firms in different industries (e.g. Almeida and Kogut 1999, Oetll and Agrawal 2008). This latter aspect is of course especially important when we study a large multinational firm as AstraZeneca and its influence on the relatively small Swedish economy.

Spread of knowledge occurs when a firm recruits a researcher from university as well as when it hires experienced persons who have previously worked in another firms. In a similar manner knowledge is transferred to the rest of the economy, when employees leave a firm for employment elsewhere in the economy (e.g. Zucker, Darby and Brewer 1998, Johansson and Karlsson 2008, Andersson and Thulin 2008). This phenomenon is recognized as an important stimulus to economic growth both in microeconomic and macroeconomic studies. These knowledge flow effects of labor mobility should be important for all types of employment, although the conscious deliberations of a firm are more systematic when it concerns recruitment of R&D workers and R&D managers.

During a normal year in recent time, the employment turnover of AstraZeneca in Sweden has been around 5-6 percent. This means that approximately 600 persons

annually leave the Swedish units to be replaced by about the same amount of new employees. In the company's R&D activities the turnover of personnel is clearly lower, with a figure varying between 2 and 4, which implies that the research team is renewed by at least 70-100 persons on a yearly basis. The corresponding inflow of new R&D workers is vital for the company's knowledge renewal, bringing in additional competencies and experiences as well as specialist skills.

The prime sources for attracting Swedish researchers are universities around the country, with the three metropolitan regions as the most important suppliers. But the company also recruits a smaller part of the R&D workers from other firms in Sweden. This latter recruitment pool refers to companies that are not competitors on the markets for drugs, although they compete for the same labor force.

Interviews with managers of AstraZeneca in Sweden reveal that recruitment from Swedish universities has to be an act of balance. On the one hand the company wants to associate prominent researchers with its R&D activities. On the other hand there is also a clear cut need to ascertain that the very best researchers in the Swedish research community can remain in their positions of performing first class research and to continue to generate a sequence over the years of young competent researchers. The capacity of securing this reproduction process is equally important already for the medium-term demand for new researchers.

AstraZeneca's annual recruitment of researchers from abroad combines to much thinner flows of new competence into the company. This can be viewed in Table 5. The annual inflow of persons from the Nordic countries and the rest of Europe has in recent years been around 6-8 in number. A small amount comes from North America. However, it should be observed that there is a fair amount of researchers in AstraZeneca in Sweden where the inflow has its origin in places outside Europe and North America. The estimation of this report is that in 2007 the Swedish R&D units employed about 425 persons with foreign background.

Tabell 5. AstraZeneca's annual recruitment of researchers from abroad, 2005-2007.

Inflow of foreign researchers	***Annual recruitment***
From other Nordic countries	3-4
From the rest of Europe	3-4
From North America	0.2

Researchers who leave the R&D sites in Sweden find their way to new jobs outside Sweden, in other Swedish companies, and to some extent also to Swedish universities. Only a very small amount disappears to academic research in Sweden, and this is primarily caused by wage compensations that are limited compared to the wage level in the pharmaceutical industry. The largest share of persons who leave from AstraZeneca R&D units get employment in other companies in Sweden, and this is evidently an important aspect of the company's knowledge diffusion to the rest of the Swedish economy. Today, a considerable number of former employees of AstraZeneca have leading positions in small and medium-sized pharmaceutical and biotechnology firms.

Experiences from the pharmaceutical industry tell us that the pertinent R&D activities are very dependent on a small number of key persons and researchers with edge competencies. Managers of AstraZeneca report that any loss in this category of persons has profound effects, because those who leave also attract skillful colleagues to follow them on their new endeavor.

Recruitment of new personnel to the company is the most decisive type of investment decisions that it has to do. The main source of information for these continuing investment choices is what can be retrieved from the company's broad and far-reaching informal networks. These networks play a role both when the company strives for staff renewal and when it searches for collaboration partners. More than 40 percent of the recruitment events are based on person-to-person information and second-order information from the established channels of the company's

communication network. As a consequence, the maintenance of this network is vital and crucial. The network is one of the company's most basic resources.

The networks that we are discussing are important not only for recruitment from the academy and other research units, with which the company has established research collaboration. The informal networks are equally important for recruiting persons who are employed by other companies. One additional argument put forward in interviews has to do with the smallness of the country, implying that is possible to have an overview of recruitment options inside the country.

7. CONDITIONS FOR PHARAMCEUTICAL R&D IN SWEDEN

A sizeable share of AstraZeneca's total R&D budget is handled by units located in Sweden. The pharmaceutical research in the country has since the middle of the 1900s benefitted from an environment characterized by first class research in medicine and healthcare, including good conditions for clinical tests as well as other forms of collaboration between the pharmaceutical industry and the health care sector. AstraZeneca's R&D units in Sweden have for a long time developed close relations to university and hospital research and continues to be favored by high research competence in Sweden. The pertinent R&D activities are not dependent on only a few top researchers, but can rely on a broad set R&D experience in the pharmaceutical research areas.

In the most recent ten-year period, however, several reports signal that Sweden is losing grounds in fields which are essential for attracting and retaining private investments in pharmaceutical research. Examples of such reports include studies initiated by the Swedish Research Council (Vetenskapsrådet) and the project *Medicine for Sweden (Medicin för Sverige*, Arvidsson et al. 2007*)* at the Centre for Business and Policy Studies (SNS). Also, a recently published SOU examines the conditions for clinical research in Sweden (SOU 2008:7).

This chapter presents an overall picture of the pre-conditions for pharmaceutical R&D in Sweden. The major input for the presentation is a series of interviews with persons working in AstraZeneca in Sweden, primarily managers in different areas.[14] They have been asked to comment on the R&D environment in Sweden and to express opinions on how the Swedish R&D units can keep their current status and even strengthen their future role in the Swedish economy and research milieu.

[14] A list of interviewees is presented in Appendix.

7.1 Supply of labor to pharmaceutical research in Sweden

A research milieu with diverse and deep discipline knowledge

The development of the pharmaceutical industry depends on the universities' basic and applied research in the biomedical disciplines, as well as the industry's need and demand oriented research, and the research on therapies and drug treatments conducted in the health care sector.

The pharmaceutical sector, including the biomedical industry, operates in a special environment, where the public sector provides financial resources to basic research, creating knowledge which is fundamental for pharmaceutical and other biomedical firms, and where the county councils (landsting) have a formal as well as practical influence on activities in the university hospitals, including applied, clinical research. If the university research becomes too narrow or thin in focal areas, the R&D environment weakens, and that perturbs the conditions for R&D intensive firms. Reduced variety and depth lowers the probability of novel products – especially when these are based on combinations of several different knowledge fields. In view of this, the decisions made by the state and the county councils have a long run impact on research strategies.

A similar type of reasoning can be applied to the education of persons specialized in chemistry, biology and medicine as well as combined fields such as biotechnology, informatics and biochemistry. Also in these cases the industry demands both many-sidedness and depth, where the pharmaceutical firms make use of opportunities to stimulate different specialties to join forces in R&D projects. The presence of multi-disciplinary competence is a prerequisite for this role of each pharmaceutical firm as an orchestrator.

Supply of researchers to pharmaceutical R&D

The opportunities to recruit competent researchers can be classified as the most essential location factor for a knowledge and R&D intensive company as AstraZeneca. Without a sufficient supply of researchers in a given location, this place becomes an impossible host region. Interviews of R&D managers in AstraZeneca reveal that the company currently perceives the possibilities to recruit young researchers as comparatively satisfactory, although some worries exist with regard to certain disciplines, for example pharmacology and pharmacy.

The interviewees in AstraZeneca express a concern about the development of resources for medical research allocated to the universities (faculty resources) during the past 10-15 years. These resources have continued to shrink. Some studies indicate that in the period 1990-2000 the basic research funding of the medicine disciplines were reduced by 20 percent, in constant prices (see e.g. SOU 2008:7). Another observation is that there are too few post-doc positions available, and this reduces the attractiveness of selecting an academic research career. In the long term these circumstances may hamper the influx of PhDs to the Swedish research environment. In particular, the share of physicians that engage in research has been falling in recent time, while a large share of physicians with a PhD is entering retirement in the next decade (Arvidsson et al. 2007).

Supply of research leaders to pharmaceutical R&D.

AstraZeneca has a recurrent need to recruit persons with both knowledge depth and research experiences. Several representatives for the industry claim that this is a particular feature of pharmaceutical research. In other industries the individual firms can more easily transform young engineers to fit the research qualifications specific to the own firm, primarily through “on the job training”. However, an R&D active pharmaceutical company as AstraZeneca has to rely on the possibility to employ

persons embodying specialized knowledge and experience in pre-clinical research. When young researchers are employed in clinical research they have to go through a costly education process inside the company to acquire the necessary competence and skills that characterize industrial drug development.

Due to its size and internal resources AstraZeneca has the capacity to train their clinical researchers in a manner that is too demanding for smaller pharmaceutical and biotechnology firms. At the end of the day, this implies that AstraZeneca partly has the role of an "industrial university" for the pharmaceutical sector as a whole in Sweden. The company is in fact the recruitment source for both new and growing firms and academic research. A large number of persons previously employed by AstraZeneca can currently be found in research leading positions in small pharmaceutical and biotechnology firms as well as in academia and authorities of the health care sector.

A general conclusion from the interviews with leading persons in AstraZeneca is that the company's recruitment of research leaders is problematic. In transparent terms: the company requires persons with experience acquired from work in other pharmaceutical firms. Such recruitment can only occasionally be made in Sweden, since there are no other large pharmaceutical companies in the country. Ever since Pharmacia disappeared from the scene, the recruitment of research leaders has become a matter of import from abroad. Obviously, recruitment of foreign candidates for research leader positions is hampered by both the low Swedish wage levels and high income taxes as considerable friction factors.

The pharmaceutical industry also voices its concern about university wage levels, claiming that the attractiveness of university research is diminished by low wage premiums. Other observations focus on the small career advantages for physicians with research ambitions and on the falling priority given to hospital research.

The described conditions imply that AstraZeneca managers have chosen to combine two measures. The first is to spend considerable resources on internal education of research leaders. The second, complementary measure is to import research leaders from other companies in primarily European countries.

The option to recruit research leaders from abroad is characterized by a whole set of friction factors, such as the Swedish wage level, the level of income tax, and cultural differences. The interviews with the AstraZeneca staff suggest policy changes as a means to facilitate the recruitment of foreign research leaders. These measures include a prolonged period for which the so-called expert tax is eligible (reduced income tax for foreign "experts"), and a less complicated rule system for the pertinent foreign-expert recruitment process. In this context the AstraZenea interviewees refer to a recent proposal from the Invest in Sweden Agency. The industry expresses a demand for a prolonged period for expert taxation as one measure. A second ambition is to get rules which are more succinct in the classification of the category "expert". In short, there is a demand for transparency and clear descriptions which are easy to grasp.

Managers of AstraZeneca point out that the obstacles of the recruitment process for foreign researchers severely reduce the attractiveness of sites in Sweden. They also put forward observations showing how other countries manage to attract investments in new R&D sites by offering various extra benefits designed to outcompete alternative locations. One such example concerns AstraZeneca's new research unit in Quebec in Canada. The overall message is rather that different regions of the world may enter into constant competition for new R&D sites.

7.2 Conditions for R&D collaboration and the Swedish research environment

Collaboration with hospitals and university hospitals

Firms developing drugs and other medical products express a wish for smooth forms of research collaborations with both health care providers and universities. Firms in the industry find that research interaction has become more complicated and less harmonious, while making reference to a better situation in the past. A major change, as expressed in interviews, is that health care authorities have adopted objectives which give strong priorities to care and treatment aspects, whereas the goal to improve treatment by means of research and development is put in the background to a greater extent than previously. As a consequence, the knowledge creation task related to clinical research tends to be constrained.

AstraZeneca's managers in Sweden emphasize that Sweden historically has been a forerunner in stimulating physicians with research interest to carry out their clinical research on patients in collaboration with pharmaceutical firms. The descriptions of the current situation contain remarks saying that productivity in treatment procedures are stressed on the behalf of research-based quality improvements. It may be that this issue of a tradeoff between short-term productivity and long-term quality development can be discussed from alternative angles. What remains is an impression that the pharmaceutical industry's opportunities to carry out clinical research in Sweden have evolved into less smooth conditions than previously. Such a view implies that Swedish R&D sites are classified as less attractive than competing locations outside Sweden.

In the book *Medicine for Sweden* (Arvidsson et al. 2007), the authors remark that the EU rules for procurement processes, with narrow constraints, may have become an obstacle for informal collaboration, and thus weakened the informal interaction. According to this view, the healthcare sector has become a less important partner in development projects of firms in the pharmaceutical and medical technology sector.

Another recurrent concern put forward in interviews with the staff of AstraZeneca is that in preceding decades Sweden has been a healthcare area in which new therapies and techniques were introduced early in the life cycle of new pharmaceutical products and related technologies. The assessment is that during the last 5-10 years Sweden has switched to become a late adopter. What is lacking is a manifest demand for improvements of existing products and development of new ones. A related issue is that healthcare studies tend to be narrow, neglecting to assess the entire value chain. Research by Frank Lichtenberg at Columbia University in the US has shown in a series of studies that using new drugs normally results in a situation where the total treatment cost falls, even if new drugs have a higher price (Lichtenberg 1996 and 2000).[15]

The importance of early adopters of new technology has been advocated in the following way. If a new drug proves to be successful in, for example, the home country, this provides information to administrators of health care in other countries, where the producer applies for approval. In view of this, AstraZeneca deplores that Sweden has moved into the group of countries with a delayed introduction of new medical technologies. In this respect, the period 1980-2000 is described as an ideal situation with mutual trust between the pharmaceutical industry and the healthcare sector. At the same time, one admits that the new so-called Ethical Agreement partly pushes things back to a better and more smooth interaction.

Clinical research and clinical tests in Sweden

The healthcare system remains an essential collaborator for the pharmaceutical industry, by performing clinical tests of new substances and treatment methods. Thus, it is vital for these clinical activities to have a clear support from the head of each hospital region. Another vital factor is the incentives of the doctors, nurses and others

[15] Gassman et.al (2008, p. 12-13) write ”because of the critical situation of the healthcare sector in most developed countries, we have seen administrators use a blanket approach to curb healthcare costs, ignoring the potentially compensating effects of new drug use.”

to participate in the research activity. If physicians lose interest in qualifying themselves in the research community, the Swedish hospitals will be less meaningful to have as collaborators.

Clinical research has been described as the link between the laboratory and good medical treatment. The feedback from clinical tests and drug development plays an important role in the process of getting approval of a new medicine as well as its introduction into regular use. The literature on this issue suggests that the described feedback mechanism functions better when the pharmaceutical firm and the hospital or clinic are located in the same region, allowing for frequent face-to-face contacts.

AstraZeneca's view as given above gets a certain amount of support in a recent report on measures to improve the clinical research. In SOU 2008:7 it is stated (p. 125):[16]

> "During recent years a set of actors have pointed at circumstances which indicate that clinical research in Sweden operate under considerable difficulties, to such an extent that it is losing in quality. Among predicaments, there is lack of time, insufficient recognition of research qualification, dismal career tracks, and slow administration procedures. The industry complains about too few research-active doctors, with declining interest in clinical tests. The head administrations mention difficulties in implementing research results. Universities signal the need for increased resources and fragmented sources for financing research."

R&D managers in AstraZenca suggest that the competence of performing clinical research is gradually undermined, and conclude that this development is serious for the pharmaceutical industry in Sweden. Comments from persons outside the company also report that a Swedish tradition in the field is fading away. At the same time, the Swedish healthcare environment does not play a major role for clinical tests. Recent statistics from Läkemedelsverket (Medical Products Agency) verifies that drug tests

[16] Freely translated from Swedish into English. See also Deiaco och Melin (2006).

have declined from more than 600 per year in the middle of the 1990s to around 400 in the beginning of the 2000s. In particular, tests in phase 3 have reduced.

The interplay between the healthcare sector and the pharmaceutical industry has become more troublesome in several dimensions in recent years.[17] The previously informal and smooth interaction has become more formal and businesslike, partly because the healthcare administration has started to charge for their services in association with clinical tests of drugs, and to view the tests as a particular service production offered by hospitals. As a consequence, informal interfaces deteriorate. An additional complication arises, because it is often ambiguous to identify who the "business partner" is. Is it the researcher, the head of the hospital administration and/or the university? In such situations the organization and the distribution of responsibilities get unclear. The outcome is a multi-party game.

In view of the described difficulties, the current state is affected by uncertainties, which disturb the associated investment decisions. Our conversations with various decision makers bring us to the conclusion that the pharmaceutical and biotechnology industries would like to see a long-term national strategy for the future conditions of the biomedical industries and the associated research milieu.

Collaboration with university research

Previous chapters describe AstraZeneca's rich collaboration network with links to several university departments and other research actors. The assessment from the company is that new friction factors have entered the picture. Previously smooth interaction lead to useful knowledge flows. A new phenomenon is that universities have developed ambitions to become leading partners in the innovation process, with a stronger focus on patenting and commercialization of research results. These new ambitions bring friction into the interaction between private industry and the universities.

[17] Regeringskansliet, DS2003:56, p. 69-70.

At the same time university researchers complain about reduced time and resources for quality research. Increased administrative burdens and stronger demands with regard to applications for research grants have similar negative impacts on research. Actual research time declines. All in all, these observations indicate that the rules of the game generate disturbances in the interplay between the industry and the universities, affecting the whole process from initiation to commercialization. Research on innovation and creativity suggests that knowledge exchange and creation is favored by reliable rules.

7.3 Do spatial clusters matter?

Multinational pharmaceutical companies in small countries must to a large extent rely on knowledge flows and input deliveries from the rest of the world. The development of pharmaceutical and biotechnology firms in a country is strongly influenced by the R&D milieu that the country is capable of affording. The most critical local environment factors are the supply of educated labor with diversified knowledge specialization. In this context, there is also a matter of critical masses for each knowledge resource.

According to an investigation made by the Swedish Governmental Agency for Innovation Systems (VINNOVA), there are about 40 000 persons in Sweden who work in around 800 firms within pharmaceuticals, biomedicine and medical technology, where more than half of the persons have research related jobs. UK, Germany and France have all a larger number of pharmaceutical firms, and that implies that these firms have a richer fund of specialists to turn to in their recruitment efforts. In Sweden each particular market tends to be quite thin, especially with regard to attraction of persons selected for research leading positions.

During the past 10 years one can observe how an impressive cluster has developed in the Washington DC region, and this illustrates a process in which public orders and purchases and proximity-based cooperation between many small and medium-sized biotechnology firms has generated a renewal and expansion of a partly new industry, with strong association to the pharmaceutical area.[18]

AstraZeneca has collaborative projects with a number of small enterprises in Sweden, where approximately 10 percent of these joint efforts are successful. In this context, the company mentions the role of VINNOVA in arranging interactive efforts, where different disciplinary competencies are combined. It is considered important to stress that VINNOVA has been helpful in accepting a longer period for basic funding in several projects. As this area comprises about 800 firms, there should be evident conditions for additional collaboration projects which aim at combining complementary pieces of knowledge. Such projects can give rise to spillovers and diffusion of ideas, strengthening the pharmaceutical and biotechnology industries. From interviews and other documentation it is also possible to conclude

- Bringing new firms into the Göteborg region would especially favor the historically advantageous R&D activity in this region (Mölndal), which for the moment lacks the desirable diversity.

- "Medicon Valley" in the Malmö-Copenhagen region has the potential of developing into a future R&D milieu, where many new biotechnology firms may emerge.

The international literature on innovation processes in the pharmaceutical industry conclude that the national context has a special role to play, with its common regulations, norms and networks. A great variety of firms of varying size in a country fosters both the innovation processes and the recruitment options. Saying this, corresponds to emphasizing the importance of the national rather the regional milieu. It seems likely that co-location of firms in the same region still should be of importance. Anyway, the local milieu is essential from other perspectives.

[18] An intriguing story about this development is provided in Feldman and Francis (2003).

Researchers who move to any of AstraZeneca's three R&D sites must find their ways into social networks and appreciate the place where they live as attractive – usually as an environment for a many-person family. As a consequence, amenities, cultural characteristics and school conditions become vital. In this context, we have observations which indicate that neither the Malmö nor the Götebrog regions appear to be sufficiently attractive for researchers that come from outside the Nordic countries. In the case of Malmö, recruitment of researchers from Denmark seems to be free from acclimatization problems.

AstraZeneca would indeed benefit from a more intense exchange between researchers in Sweden and the US. The type of environments that develops in regions like Boston, Washington DC, San Francisco and southern California generates clusters of researchers who benefit from their mutual interface, also when they represent fairly disparate disciplines. Research institutes have developed to strong attractors of talents from all different parts of the world. The aspired development in the Malmö-Copenhagen region can be viewed as attempt to follow similar paths as those in the USA. In the Stockholm region there are likewise efforts to form the Stockholm-Uppsala Bioregion.

7.4 Strategy for Sweden as a pharmaceutical research milieu

There is a clear demand or wish for a long-term national strategy, designed to promote the development of the pharmaceutical research environment in Sweden. Interviewed person in the AstraZeneca company argue that politicians and other decision makers have to contemplate the national importance of hosting large R&D intensive companies. A major, economy-wide spillover effect that springs from hosting such companies in Sweden include impacts on the labor market providing career opportunities for knowledge-intensive labor, and stimulating university research.

Representatives of AstraZeneca argue that the company would benefit from long-term visions of the future R&D system in the country. The company would like to see a

national policy which pays special attention to research issues. Such a vision could function as a platform for discussion and exchange of ideas with focus on the future of the pharmaceutical industry. An ideal from the company's viewpoint would be recurrent round-table discussions. To illustrate this there is a reference to earlier discussion of this kind, which resulted in the programme *Pharmaceutical products, biotechnology, medical technology – a component of Innovative Sweden.*[19]

[19] Läkemedel, bioteknik och medicinteknik – en del Innovativa Sverige

8. CONCLUSIONS AND POLICY SUGGESTIONS

The external environment is important for both the pharmaceutical industry and biotechnology. In Sweden the industry is strongly affected by policy decisions. This can be illustrated as follows:[20]

- Because of public financing of the universities, the state is responsible for a large fraction of the industry's science and knowledge base
- The system for undergraduate studies is shaped by the state
- Firms that develop new drugs and medical equipment depend on the conditions for collaboration with the public healthcare sector
- The development and the introduction of new drugs and medicines are surrounded by public regulations
- A large share of the costs for drugs and medicines is financed by the state and healthcare authorities.

The location and capacity decisions of large research intensive multinational companies like AstraZeneca are based on the location conditions in different regions world-wide. Each region's location characteristics include the possibilities to recruit researchers, cooperate with leading research institutions, conduct clinical tests and collaborate with hospitals in a variety of other ways. The global perspective implies that locations in Boston, Montreal as well as regions in China and India are compared with Sweden, the Malmö, Göteborg and Stockholm regions in particular. As illustrated by recent research, proximity to markets as well as knowledge sources play a role in such comparisons, although the latter motive has grown in importance.

[20] See Arvidsson et al (2007 p. 13-14).

The data and analyses presented in this report illustrate that AstraZeneca plays an important role in Sweden, in particular for the Swedish knowledge economy. The company appears as a significant part of the Swedish economy from different perspectives. This may motivate more than just general economic policy. The company accounts for example for a significant share of Sweden's exports, both in the form of exports of manufactures and services. The large export flows contribute substantially to the country's net exports.

Our analysis of the Swedish units' interaction with the rest of the Swedish economy shows that 'traditional' couplings in the form of transactions with Swedish suppliers are limited. It is instead the company's position in the 'knowledge economy' that makes its presence in Sweden important.

- The calculations in the report show that about 15 percent of the total business R&D expenditures in Sweden can be attributed to AstraZeneca's units in Sweden.

- If one looks at AstraZeneca as a research unit, the company's units in Sweden conduct R&D man-years in the same order of magnitude as the Karolinska Institute and more than the Royal Institute of Technology. Expenditures on collaboration projects with Swedish universities amount to about two thirds of the research budget of a regional university with about 10 000 students.

- The company's demand for hospitals to participate in different types of projects, such as clinical tests and other knowledge feedback, provides a basis for medical research in Sweden. The collected material in this report suggests that this potential is not fully developed. Medical research has historically been a scientific 'flagship' of Sweden.

- For the triangle Stockholm-Göteborg-Malmö the company can be described as an 'anchor-tenant', i.e. a large firm which demands specialized inputs, in particular knowledge flows and highly educated and skilled workers. To the extent that proximity is important for these flows, it gives a potential for (i) advanced university education and (ii) the establishment of smaller companies with couplings to the anchor tenant. There are thus possibilities for new biotechnology firms to take

advantage of and contribute to AstraZeneca's R&D projects. To develop a strategy for such renewal of Sweden's pharmaceutical industry should be a mission for AstraZeneca. A spillover effect from the company's activities in Sweden is that it 'educates' entrepreneurs as well as potential workers in new biotechnology firms. Such strategic outsourcing could be the most promising opportunity for AstraZeneca to establish and design its own R&D environment.

The challenges and strategic issues faced by pharmaceutical companies described in the report imply that the industry will go through structural changes. The strategic choices for pharmaceutical companies comprise a large set of factors. For Sweden, an important consequence is that the companies need to make location choices and build networks that secure accessibility to knowledge, embodied by universities, biotechnology firms and other pharmaceutical firms.

- Locations in Sweden must be attractive for firms as well as individuals. The possibilities to attract foreign researchers are important but problematic for the Swedish pharmaceutical industry. A critical question for research is to clarify which characteristics in a local milieu that make it attractive and stimulate foreign workers to remain in the milieu, while developing durable social networks.

- In a longer perspective, the density of pertinent firms in the Swedish environment is an important location characteristic. Biotechnology firms are for example becoming more important as knowledge sources and collaboration partners for the large multinational pharmaceutical companies (Rothaemel 2001, Gassman et al 2008). There is a large international literature analyzing the role of clusters of biomedicine and biotechnology firms as well as the role of networks for R&D and knowledge transfers for pharmaceutical firms. This literature is however not systematized and structured in such a way that it can be used for the formulation and design of economic policy in Sweden. In this perspective, there is a relevant Swedish research area. Existing knowledge suggests that there is role for economic policy to create an infrastructure and incentives for expansion and cluster formation among small biotechnology firms. Feldman and Francis (2003, p. 765) draws the following conclusion about the development of the biotechnology cluster in Washington DC in the US: "The Capitol region biotechnology cluster, in essence, is the result of three

reinforcing sets of factors: pre-existing resources, entrepreneurship and the incentives and infrastructure provided by government".

For the pharmaceutical companies the possibilities to recruit highly qualified personnel is a critical location factor. This is affected by the education systems (including graduate studies), by the conditions for doctors and other employees within the healthcare system to conduct research as well as by the possibilities to recruit personnel from abroad. The analyses and data in this report suggests that there are strong reasons to:

- Increase faculty allowances to earlier levels in pertinent research areas as a first step towards the goals in the Lisbon agenda of public R&D at the level of 1 percent of GDP.

- Undertake measures to strengthen and facilitate the clinical research in Sweden

- Consider a prolongation of the expert tax subsidy, for example from the current three to five years. Also, the legislation could be developed such that it becomes more transparent and understandable. There are also reasons for a more generous application time such that firms can apply for tax reductions for foreign experts that have already worked in Sweden for a certain period of time.

- Develop simpler procedures for recruitment of personnel outside the EU. New possibilities may open up when more highly educated people from Asia and other parts of the world enter the global labor market.

- Work for a society that is inclusive for immigrants.

The Swedish pharmaceutical industry's ability to compete for leading researchers is paramount for the industry's long-term future in the country. Such ability requires an administrative, economic and social environment which makes it possible to attract

researchers with work and research experience from any of the world's leading research milieus.

The milieus that have developed in Boston, Washington DC, San Francisco and southern California generate a cluster of researchers that benefit from each other despite disparate disciplines. These research milieus attract talents form all over the world. The ventures in Malmö and Lund in collaboration with Copenhagen and Odense are an attempt to imitate the development in the US regions. A corresponding venture currently takes place in Mälardalen, i.e. the Stockholm-Uppsala Bioregion.

The triangle Stockholm/Uppsala-Göteborg-Malmö/Copenhagen corresponds to many of the US regions and some of the EU regions when it comes to R&D networks and interaction. There are thus two layers of the region concept:

1. The first type of region should be a base for frequent interaction between researchers at universities, healthcare institutions within the biomedicine and biotechnology areas firms. Such an R&D region can comprise that whole Swedish "pharmaceutical triangle".

2. The second type of region is much more local in nature and relates to its attractiveness as a place of settlement for Swedish and foreign researchers.

The following statement by Malecki (2004) illustrates that importance of attributes and amenities that make regions attractive for highly educated and skilled individuals:

> "The latest priority is being placed on attracting mobile workers and mobile investments. Creative workers are the core of the knowledge economy [….] Lists or league tables of 'the best place' to live, to retire and to visit are key features of economies or societies whose factors of success are highly mobile [….] Competition among places involves more than marketing or attempting to sell them. It involves the enhancement or improvements in the attributes that make it possible to attract and keep investments and migrants – that is, to become 'sticky places'." (Malecki, 2004 s.1101 and 1103).

It is of course a long way before anything that corresponds to the large US research milieus is developed. It is also unclear to what extent milieus of this type can be planned. However, initiatives to develop competitive research milieus can be critical for the long-term future of the Swedish pharmaceutical industry.

The conclusions so far have pointed to an increase in the faculty allowances for pertinent research areas, the conditions for clinical research, adjustments in the expert tax subsidy, the planning of functional regions as attractive places of settlements, etc. Other conclusions are:

- Swedish industrial and R&D policies should contemplate developing conditions that can facilitate the formation of R&D networks for the discovery and development phases of the pharmaceutical industry. An important issue is the collaboration opportunities between pharmaceutical companies and the healthcare system, including university and other hospitals. A related issue is communication at early stages about which treatments, for which the healthcare system is willing to pay.

- Health economic cost-benefit assessments should be developed to cover the whole value chain. This may require a standardized and sanctioned method of analysis – where priority should be given to completeness and transparency.

- The legal conditions for stem cell research in Sweden are considered to be favorable from a research perspective. In combination with Swedish rules for bio banks the favorable conditions is a typical example where there is an option for developing and industrial policy.

- There are established experiences in Sweden of so-called round table discussion between government and industry. Since the pharmaceutical industry as well as the healthcare system in Sweden are highly dependent on public decisions, there are arguments in favor of this type of interaction as a means to provide visions for the future.

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APPENDIX – list of interviewees

The AstraZeneca individuals interviewed for this report were executive leaders of the company´s operation in Sweden:

- Head of Sweden Operations
- Head of Sourcing and Supply Management
- Executive Vice President, Head of Global Discovery Research
- Head of Turbuhaler and API
- Vice President Human Recourses
- Assistant General Counsel, Legal Department
- Vice President, Global Safety Assessment
- Director Clinical Project Coordination
- Vice President and Global Product Director, CVGI Therapy Area
- Global Vice President Research Area CV/GI
- Vice President PA R&D
- Vice President Global Discovery Research Area CNS/Pain
- Marketing Company President Sweden
- Head of Sweden Purchasing
- Business Analyst R&D Operations Finance
- Vice President Clinical Sweden
- Chief Financial Officer
- Vice President Discovery Information
- Regional Director Medical Science

Additional interviews were done with former executives of AstraZeneca, individuals now in new positions outside the company, and with external experts in relevant fields.