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The Pharmacia Story of Entrepreneurship and as a Creative Technical University – An Experiment in Innovation, Organizational Break Up and Industrial Renaissance

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THE PHARMACIA STORY OF ENTREPRENEURSHIP AND AS A CREATIVE TECHNICAL UNIVERSITY[1] -an experiment in innovation, organizational break up and industrial renaissance

by

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Abstract

While innovative technology supply has been the focus of much neo Schumpeterian modeling, few have addressed the critical and more resource demanding commercializing of the same technologies. The result may have been a growth policy focused on the wrong problem. Using *competence bloc theory* and a firm based macro to macro approach we abandon the assumed linear relation between technology change and economic growth of such models, and demonstrate that lack of local commercialization competences is likely to block growth even though innovative technology supplies are abundant.
The break up, reorganization and part withdrawal of Pharmacia from the local Uppsala (in Sweden) economy after a series of international mergers illustrate. Pharmacia has "released" a wealth of technologies in local markets. Local *commercialization competence*, notably industrially competent financing has, however, not been sufficient to fill in through indigenous entrepreneurship the vacuum left by Pharmacia. Only thanks to foreign investors, attracted by Pharmacia technologies, that have opted to stay for the long term the local Uppsala economy seems to be heading for a successful future.
The Pharmacia case also demonstrates the role of advanced firms as "technical universities" and the nature of an *experimentally organized economy* (EOE) in which business mistakes are a natural learning cost for economic development.

Key Words: Competence Bloc Theory, Commercialization of Innovations, Experimentally Organized Economy, Innovation and Entrepreneurship, Pharmaceutical industry

JEL Code: L2, L65, M1

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[1] This paper draws directly on a larger study of the Lake Mälar regional economy in Eliasson (2005a) and Eliasson-Eliasson (2002 a,b.c). It was originally prepared for the ISA session at the conference *Förändringens Vindar och Vanans Makt,* Piteå, Sweden 18-20 August, 2004. Revised versions have been presented at seminars at ERMES, Paris Universite II –Pantheon-Assass, on Jan 17.2006, at the Ratio Institute, Stockholm, on March 29. 2006 and at MERIT, Maastricht on May 2. 2006. We are very grateful for a number of useful comments from Gerard Ballot, Niclas Berggren, Andreas Bergh, Robin Cowan, Gissur Erlingsen, Dan Johansson, Nils Karlson, Henrik Lindberg, Pierre Mohnen and Luc Soete. Many thanks also go to the large number of people interviewed in Swedish firms. Without their contributions this study would not have been possible.

1. Entrepreneurship and the Local Commercial Environment - Competence Bloc Theory

Local *receiver competence* (Eliasson 1986, 1990a) and *absorptive capacity* (Cohen-Levinthal 1990) are terms used for the competence to develop, identify and support winning technologies and to take them on to industrial scale production and distribution. While technologies are internationally available the industrial outcome depends on the local competence to commercialize them.

In the Uppsala regional economy, the case we will present, Pharmacia has been a prolific supplier of innovative technologies for almost a century, but not necessarily a competent commercializer of the wealth of innovative technologies it has created. It has very much, and inadvertently operated as a successful technical university and has had the same problem as universities have had of commercializing the new technologies they have developed. In fact, for Sweden at large, and the Uppsala region in particular, *innovation and technology supply appears to have been no problem.* The problem has been the local competence to commercialize the new technologies through entrepreneurship (Eliasson 2003, 2005a). The nature of the commercialization competence is the focus of competence bloc theory and of this paper.

Distributed production, furthermore, is rapidly making the notion of a firm a formless entity constantly changing its internal structures and outer limits in response to changing market conditions (Coase 1937, Eliasson 1996b, Eliasson- Eliasson 2005). Much of this is taking place through mergers and acquisitions (M&A), turning previously internal reorganizations into open market transactions. With the structural recombinatorics of firms increasingly taking place over the market, a new and broader agenda of opportunities for creating winning business entities is opening up, but to do it right is very competence demanding of management, and frequently leads to failure. Two questions will, therefore, be addressed:

1). Will the total industrial outcome after Pharmacia´s break up and the release of internally developed technologies in the market be more or less total output? and

2). Will that output be located in the Uppsala/Lake Mälar (Stockholm) region or elsewhere?

To assess the alternative regional outcome through new entrepreneurship based on technologies spilled from Pharmacia the results from case studies have been used. To integrate the results from these case studies into a consistent regional analysis, a new type of dynamic theory is needed which is not part of the standard agenda of economic analysis.

Under the conditions the theory of the *Experimentally Organized Economy (EOE)* and of *competence blocs* [2] we expect the transformation paths of the Uppsala region to be strewn with business failures most of which are needed to create a few winners. If local entrepreneurial conditions are not right, no winners may be identified and regional stagnation follow. In fact, many observers from both the political and industrial Uppsala communities have been worried about the disappearance of the only large local industrial player. One question, therefore, is: Is commercialization of new technologies through big companies more efficient than through new entrepreneurial establishments?

A dual logic has determined the structure of this paper, which is organized around the Pharmacia case. One property of the EOE is that even at known relative prices there always exist better (more productive) allocations of resources than the existing one. To be achieved, however, new competencies are required. If the resources are freed from the existing allocation and subjected to a more competent evaluation a better allocation, therefore, is achievable if the economic and institutional environment is congenial to entrepreneurship, but a worse allocation is also a possibility.

This paper "tests for" a positive version of this *Shake Loose Hypothesis* that can be derived from the theory of the EOE. Hence, the theory should logically come before the empirical presentation of the case. The theory of the EOE, however, rests on one fundamental informational assumption that sets it apart from the mainstream economic model, namely that the state of full information is unattainable, that actors are in general fundamentally ignorant about circumstances that may affect their survival and constantly commit business mistakes. The latter is a postulate of old Austrian economics, notably of Menger (1871) and von Mises (1949). We can simply enter that property as an assumption- which is well in accordance with common practice in economics- or refer to other sources documenting the factual circumstances underpinning the theory of the EOE as empirically inevitable. As it is, however, the Pharmacia case is also a perfect documentation of the factual underpinnings of the same theory, i.e. of the complexity and size of the business opportunities space that makes it impossible for any actor of even coming close to what is feasible to achieve. We, therefore, ask the reader to keep that in mind when s/he reaches the case presentation, since we have decided to begin with the theory, derive the shake loose hypothesis and then proceed to test it.

Macro dynamics through Schumpeterian Creative Destruction- the theory of the EOE

[2] For more on this theory and the interviews see Eliasson (1987a,1991a,1992, 2005a,b) and Eliasson- Eliasson 1996, 2005).

When something radically new is introduced in the market it almost always occurs through the launching of a new product, the establishment of a new division or through the entry of a new firm. A new product may be a complement to existing products or a substitute, in the latter case subjecting existing producers to competition and forcing them to reorganize and/or rationalize, or die (exit). When a competitor introduces a radically new product a firm often cannot cope with the new situation through reorganization, because it is staffed with the wrong human capital. It then has to contract or shut down, and possibly recruit new personnel to establish a new firm.

Critical for the sustainability of that dynamic market game are the assumptions we make about the properties of the *business opportunities space* and about how these properties are sustained "forever". The argument, presented in more detail elsewhere (Eliasson 2005a) is that the opportunities space is sufficiently large and complex to make each individual actor grossly ignorant about circumstances that may be critical for its survival, that free access to explore those opportunities keeps each actor constantly innovating in order not to be overrun by better competitors and that the opportunities space grows from being explored through learning and the creation of new combinations of opportunities. This way the economic system maintains a positive sum game forever, through innovative exploration of the opportunities space and competition.

The dynamics of this growth promoting competition is reflected in the dynamics of rent formation in financial markets, successful Schumpeterian innovators earning a temporary competence rent that will be competed away by Kirzner (1973) type imitators or new Shumpeterian innovators; a dynamic positive sum market game that drives macroeconomic development through Table 1. As a consequence the capital market will never be in what economists call static equilibrium and the firm population will constantly feature a wide distribution of rents subjected to constant reshuffling over a variable population of incumbent and new firms (Eliasson 1984). The entry/exit process (firm turnover), hence, determines economic growth, pushing performance of the entire industry upward through the Schumpeterian creative destruction process of Table 1. Entry is moved by innovators and economic incentives as determined by the institutions in markets (see below).[3] If superior

[3] The reasoning can be illustrated using a Salter (1960) curve. See Eliasson (1996a, pp. 44 f). This is also the way growth is endogenized in the Swedish micro-to-macro model (Eliasson 1991). It is particularly important to observe that innovative entry subjects incumbent firms to competition and forces them to respond. Their response in the form of innovative reorganization or desperate rationalization may mean both expansion and

entrants and successfully reorganizing firms (the"winners") are supported by the market and allowed to force inferior firms to exit economic growth will follow. But this successful outcome requires that actors and resource providers be competently guided. The *competence bloc* performs those functions of guidance and resource provision.

(Tables 1 and 2 in about here)

Competence bloc theory

Frequent business failure in the EOE is a normal learning cost in economic development and has to be counted as part of transactions costs. The largest such cost in the theory of the EOE is the loss of a winner (Eliasson- Eliasson 2005). Dynamically efficient selection in the EOE, therefore, is defined as the "minimizing" of the economic incidence of two types of business mistakes , i.e. keeping losers on for too long and "losing the winners" (Table 2A). Competence bloc theory explains that "minimization" and, therefore, can be seen as a widened theory of the firm. The mainstream economic model (still) assumes that most knowledge has the character of codable information that can be "costlessly" (zero transactions costs) centralized to one point without loss of information. To achieve a globally efficient resource allocation, centralizing tacit knowledge to one point, however, is impossible by assumption and, therefore, reduces the main notion of full information to such codable knowledge, and/or knowledge that can be communicated at no or negligible transactions costs. Since tacit knowledge in the sense of limited communicability can be demonstrated to exist in all decision situations characterized by varied and boundedly rational decision makers (Eliasson 1990a), as is the case in the theory of the EOE, decisions on how to allocate resources cannot theoretically be centralized and analytically optimized, but instead take the form of *experimental trials in markets*. If, in addition, tacit knowledge is the critical input in higher level decisions, the irrelevance of the centralizing proposition is further emphasized. Distributing tacit knowledge (or human or team embodied competencies) over the market, however, can be shown to expose each project to a maximum competent and varied evaluation. A competence bloc (Table 2B) lists the minimum number of actors that are needed to successfully create, identify, select and commercialize new business ideas, i.e. to initiate and develop a new industry. However, more or less of the competence bloc, sometimes the entire competence bloc can be internalised within one "large firm" hierarchy. As we will

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contraction depending upon incentives embedded in the institutions of the economy and the individual competence capital of firms.

show, the nature and efficiency of project selection differs radically depending on how large a part of the selection and commercialisation that is internalised within one firm and how much that is distributed in the market. This is a dynamic version of Coase (1937). While the market based commercialization will result in a more informed and more efficient selection (G. Eliasson – Å.Eliasson 2005) it requires extensive and costly market transactions in intellectual property across the competence bloc and, hence, a much more sophisticated property rights system than most economies have developed (Eliasson-Wihlborg 2003). The dynamic efficiency characteristics of that allocation are determined through the balancing of a wider transactions cost measure that also includes the differing risks of losing winners in a more or less distributed allocation (See Table 2A and below).

The perhaps most important product feature demanded in an advanced market is product or quality *variation*. The more multidimensional products are, the more difficult it is to assess demand and to price products. The producer can guess, but he has to try his novel product in the market before he knows. Only the customers can individually decide which variant they prefer. This places the customer in core. One critical task of the competence bloc, hence, is to make sure that customers' preferences filter down to the actors in the competence bloc that create and select innovations. This requires that both customers and products be well defined such that property rights can be assigned to contractual commitments throughout the competence bloc, making trading in these commitments possible such that the right prices be signaled, losers filtered away and winners selected. *The competence bloc becomes an allocator of tacit competencies* (Eliasson – Eliasson 2005). *T*he *customer,* hence (*first*), occupies a premier position in competence bloc analysis. The products created and chosen never get better than what *customers* are capable of appreciating and willing to pay for. The long-term direction of technical change, therefore, is always limited by the customers´ ability to understand the product and willingness to pay. Sometimes the customer takes the initiative and contributes (commercial) competence to the innovation choice process. They may actively look for products that they need and accept or reject products offered to them in the market, thereby signalling what they want. They may even be directly involved, contributing knowledge to the development of a product. This is often the case when it comes to advanced and complicated products such as military and commercial airplanes (Eliasson 1995, 2001b). Technological development, therefore, requires a sophisticated customer base, capable of appreciating new products. The more advanced and radically new the product technologies, the more important customer sophistication becomes. An advanced local customer base

becomes a competitive advantage for the industrial economy. As already observed by Burenstam–Linder (1961) the customers of the rich economies contribute to their comparative advantages. In terms of competence bloc theory, local access to affluent and competent customers is a strong regional attractor for advanced firms. The once very sophisticated Swedish health care sector probably contributed to the development of a sophisticated Swedish pharmaceutical and biotech industry. Recently, however, Astra-Zeneca (DN, Ekonomi, July 21. 2004) let it be known that the company may reduce its planned research presence in Sweden if Swedish health care authorities are not interested in buying its most sophisticated products. Competent, wealthy and innovative customers probably are what keep the US health industry ahead of the rest of the world (Eliasson-Eliasson 2002b).

Second, basic technology is internationally available, but the capacity to identify it and make a business of it requires local competence. Part of this *receiver competence* (Eliasson 1986, 1990a, 1996a, pp. 8, 14) is the ability to create new winning combinations of old and new technologies (*innovation*)[4]. A rich and varied supply of subcontractor (technology) services, therefore, is part of the innovation supply that enters the economic selection process of the competence bloc through that slot.[5] But innovation supply does not make an industry.

Third, not all innovations are commercially viable. The task of the *entrepreneur* is to identify commercial winners among the broad supplies of innovations and to get the new technology on a commercial footing. The behaviour of the innovator and the entrepreneur is by its very nature unpredictable, which was also the notion advocated by the young Joseph Schumpeter (1911).

The entrepreneur, however, rarely has resources of his own to move the project forward. He, therefore, (*fourth*) needs funding from a *venture capitalist*, i.e. a provider of risk capital, capable of understanding the innovative and radically new technologies the entrepreneur is

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[4] *Innovation* is a technological concept to which the *entrepreneur* (see below) adds the economic dimension. Even though the two actors often are integrated in the same individual or firm, they represent principally different competencies. Theoretically you have to keep them apart. I therefore treat the supply of new technologies and innovation supply as synonyms. This is von Mises (1949) definition. The competence of the entrepreneur is to be able to successfully choose the potential winners from a broad supply of technologically defined competing innovations. Also the technological ability to create new technological solutions (innovations) and the economic competence to choose the profitable winners do not easily combine in the same individual or firm department. Large firms in fact often keep the two functions organizationally separated (Eliasson 1976, 1996a).

[5] Carlsson (1995, 1997) has modeled that innovation supply under the name *technological systems*. It is, however, difficult to keep a clear distinction between the physical and the intellectual dimensions of the economic system. Technology supply is often thought of in physical engineering terms even though this is a misconception. Similarly the competence bloc which governs an entirely intellectual innovation and commercialization process should not be confused with Erik Dahmens´s (1950) *development bloc.* The development bloc deals with the physical productivity improvements achievable within a production and distribution system undergoing expansion and reorganization.

promoting, identifying business needs and providing context. The money is the least important thing. *What matters* is *the industrial competence needed to understand and identify winners and, hence, provide reasonably priced equity funding*.[6]
Without a rich endowment of venture capital competence, you won't see many entrepreneurs. Hence, the venture capitalist and his escape (*exit*) *market (fifth)* are the important incentive supporting actors. With no understanding venture capitalists the price of new capital will be prohibitively high, or funding will not be available, and winners will be lost. New firms will be undervalued. With badly functioning exit markets the incentives for venture capitalists will be small and, hence, also for the entrepreneurs and the innovators. Undervaluation of sophisticated biotech firms at this critical stage not only subjects the new entrepreneurial small firms to excessive risks, but also opens up a local market for cheap strategic acquisitions by competent foreign buyers (DI Aug. 31. 2005)

Finally and *sixth*, when the selection process has run its course and winners have been selected a new type of *industrial* competence is needed to take the winners on to industrial scale production and distribution. The industrialist figures in the competence bloc on account if his or her capacity to contribute functional competence. Also at this stage winners can be lost to the local economy due to lack of management competence. Part of the regional location factors at this level, we will find below, depend on the supply of such competence. The task of identifying and carrying the winners on to industrial scale production through Table 2 is critical for macro economic growth.

The competence bloc represents a sequence of assessment and selection activities that all have to take place to make sure that winners are not lost and that losers are not kept for too long on the budget (dynamic efficiency, see below). We, therefore, conclude that *completeness* of the competence bloc is a necessary requirement for the viable incentive structures that guarantee increasing returns to continued search of winners, i.e. for new industry formation. *Vertical* completeness is one requirement. None of the "pillars" (the actors) of the competence bloc can be missing, or this complete incentive structure will fail to develop (G. Eliasson – Å. Eliasson 1996). Hence, the absence of entrepreneurship so frequently discussed to explain European stagnation may miss the point. More likely, we conclude, is the lack of industrially competent financing, without which we won't see any entrepreneurs (Eliasson 1997b, 2002b).

[6] A venture capitalist in the competence bloc is *defined* as a provider of finance embodied with such industrial competence. The venture capitalists so defined also contribute managerial, financing and marketing competence through their network, but this comes after the "understanding". Such services are normally available in the market and, consequently, are less critical; see G. Eliasson – Å. Eliasson (1996) and Eliasson (1997b, 2002b).

The extreme diversity of the business opportunities set of the EOE, furthermore, means that the competence needed to identify winners cannot be specified in advance. Hence, an efficient project identification and selection in the competence bloc requires that a large number of each type of actor in the competence bloc be present. Such *horizontal variety* is a necessary condition for *maximum exposure of each project to a competent and varied evaluation*. Compared to the internal project evaluation in a large firm, direct transactions costs may be higher, since the evaluation is done in a distributed fashion over the market, involving many independent actors. Narrowing down the evaluation to an internal procedure within a hierarchy, on the other hand, raises the risk of losing a winner which constitutes the really large transactions cost, and hence is likely to lower the efficiency of project selection (Eliasson – Eliasson 2005). This is not uncommon. Large firms, such as IBM, internalised most of the competence bloc for years and exposed themselves to a conservative project selection. Business history, in fact, is full of near losses, the only ones that can be identified (Eliasson 2001b). In a complete and horizontally varied competence bloc distributed over markets for specialized competence services *potential winners are exposed to a maximum varied competent evaluation such that they experience increasing returns to continued search for resources.*

Critical Mass Creates a Combined Local Spillover Source and Global Resource Attractor **-** *the Advanced Firm as a Combined Technical University and Business School*

A complete and horizontally varied competence bloc functions as a technological spillover source. Advanced firms are (1) attracted since they can benefit from an ample supply of complementary technology spillovers. But as they establish in the competence bloc (2) they also spill new technology to the firms already established there. In that sense advanced firms provide the same services to the economy as *technical universities*, but not only that. Spillovers also have to be identified as commercially viable and introduced into the production system. On this, we know that the advanced firms take technological innovations much closer to the market, for instance in the form of e valuated product prototypes, than a technical university is capable of. Since *the economic value of spillovers depends on the local ability (receiver competence) to commercialize the spilled technology* the advanced firm in many ways is a more efficient and valuable (to the economy) provider of new technology than a technical university. The competence bloc defines that receiver competence (Eliasson 1986, pp.57f, 95, 1990a, 1996b) at the national level, an idea discussed already by Abramowitz

(1988).

Together all this means that the full fledged competence bloc turns the spillovers created by the research and industrial activities of advanced firms established there both into ”functionally operational technical universities and business schools” and commercially viable ventures (*joint production*, Eliasson, 1996b, 2001a). Advanced firms thus compete with the established technical universities as educational institutions, providing on the job learning and experience development in a large area of production where standard educational institutions have little competence to contribute and where classroom teaching is not a viable educational method.

Commercialization competence has been demonstrated to be critical for linking technology supply to economic growth. Competence bloc theory therefore, exposes some alternative theories of economic growth, notably Schumpeterian II(1942) type linear R&D and innovation push theories to criticism by simply placing them in a more realistic context which breaks the linearity. Without sufficient commercialization competence an abundant supply of innovative technology will not result in economic growth.

Dynamic Economic Efficiency

Dynamic allocation efficiency in the EOE has to account for the implicit cost of losing a winner. The incidence of such losses increases with the narrowness of the economic and industrial evaluation, i.e. as you go from a distributed market based competence bloc to an internalized evaluation. Identifying and developing the right product for the right market defines the competitive edge of the firm and an ability to capture a high value for its products. Part of that ability rests on the capacity of the firm to flexibly change product qualities as customer preferences change.

To identify what is right ahead of changing customer tastes, however, is a formidable business competence and it is easy to err in business judgement. Winners often get lost in that process. Hence, the definition of efficiency in the theory of the EOE must be related to the identification and the development of the right products and only as a secondary concern to how efficiently they are manufactured (See discussion of different efficiency definitions in Eliasson 1985, p. 329f, 1991a, p.165). Differently expressed, the *definition of dynamic efficiency must be to “minimize” the economic consequences of committing the two types of economic errors in Table 2A,* i.e. to keep losers on the budget for too long and to lose the winners.

The absolutely best winner is indeterminate in the EOE. Formal mathematical "minimization", therefore, is not possible. The dynamics of competition sustained by large business opportunities in the EOE and free entry, however, pushes the economy towards the best possible and sustainable efficiency. Since the model of an EOE normally does not have a determinate exogenous equilibrium[7] general competition for improved positions among all actors is analogous to computing an approximate mathematical solution to an optimization problem[8]. This also defines the main difference between dynamic and static efficiency. The static model has an analytically determinable optimum that can be used as a bench mark for efficiency comparisons. The theory of the EOE offers no such external benchmark, except the knowledge that competent actors can always achieve profitable improvements at a cost. The absolute optimum is, however, unknown, or rather indeterminate. This is also the theoretical basis for the Shake Loose Hypothesis.

The Shake Loose Hypothesis

The shake loose hypothesis is viable only because of the assumed existence of a difference between the indeterminate level of dynamic efficiency and the determinate reference of static efficiency. The Shake Loose hypothesis, therefore, only makes sense within the theory of the EOE. Its rationale is partly that resources can be released for more profitable and growth promoting employments elsewhere, but also that technologies are released for better "management attention" elsewhere. Hence, a positive version of the Shake Loose Hypothesis requires that such better management attention is locally in place. This can be empirically ascertained through an assessment of the completeness of the local competence blocs. Before that, however, there has to be a rationally founded lock in.

The first critical question to be raised is whether the technological lock in hypothesis of Arthur (1988,1989,1994) or Ballot-Taymaz (1998) is a rationally founded proposition. Grossman-Stiglitz (1976,1980) demonstrated that the economy can get stuck in an inefficient equilibrium because the prices at which trade takes place may not convey sufficient information. Dixit (1989) demonstrated the existence of " rational inertia" or " hysteresis" because of sunk costs. Both propositions are staged within a standard general equilibrium model. Klepper (2006 a,b) has studied similar situations, or industrial shake outs in the US

[7] Which is typical of non-linear economic systems (Eliasson 1977, 1991a, Day 2004)

[8] This, for instance, is the procedure in the highly non linear Swedish micro-to-macro model, which has no external equilibrium, but in which actors are still guided by more or less reliable price signals in markets towards some approximate, but constantly moving focus, the location of which depends on the ongoing search (Eliasson 1991a)

television receiver and automobile industries empirically. Klepper´s focus is on spin offs caused by internal disagreements that have caused employees to start new firms in the same or similar businesses, eventually leading to immense and dynamically more efficient agglomerations of similar production in the same area, such as the concentration of automotive industry to Detroit. One could say that the informational assumptions of the theory of the EOE take in all these propositions and allow the additional conclusion of the general incapacity of the economic system of ever achieving the best of all possible allocations. Hence, our proposition one is that there always exist more (dynamically) efficient allocations of resources for each given and known set of relative prices than the current one. The positive version two of that proposition is that more efficient allocations (rather than worse allocations) are attainable under certain infrastructure conditions defined by the competence bloc. In other words, better allocations can be achieved under vertically complete and horizontally varied competence blocs and a property rights regime that ensures sufficient tradability in knowledge assets to facilitate market based allocations of such assets between the agents of the competence bloc. Testing for the shake loose hypothesis, therefore, will be performed in two steps. We first check for the completeness of the competence bloc and then proceed to do econometrics on a simple model of the Uppsala population of bio firms in which the situation of a "preserved" Pharmacia can be defined. The procedure is quite simple. Fridh (2002, Ch 4) regresses growth in employment in all biomedical establishments in Sweden between 1993 and 2000 on their age and size (both also squared), an ownership dummy (private or public), a dummy for Uppsala location and an interactive dummy that is one for exiting Pharmacia establishments. Time series and cross section data are pooled and the null hypothesis tested that the Pharmacia dummy be negative. The null hypothesis is rejected in favour of a zero or positive effect on the Uppsala economy of the Pharmacia exit.

2. The Pharmacia Case[9]

We present the entrepreneurial creation over almost a century of a new, eventually giant international corporation. It emerged through more or less successful acquisitions and failed or well managed mergers only to be broken up, radically reorganized and partly withdrawn from the local Uppsala economy during its final ten years. It was finally absorbed by two

[9] This section draws directly on a large number of interviews that the two of us have carried out together, or individually over several years that have been documented in Eliasson- Eliasson 1996, 1997,2005 and Eliasson 2001c, 2005a, Ch.V).

international giants, leaving dozens of small entrepreneurial spin offs struggling for survival in the market. Is this a recipe for local regional distress or a ticket for a better future?

We find that new, small and innovative businesses often fail at the critical stage when external venture capital is needed, because the industrial competence to understand the business is lacking in the local venture capital community. We also observe, and surprisingly so for a country known historically for its large and well managed international firms (Eliasson 1976,1991b, 1996a), that the local ability to take potential winning technologies in new industries on to industrial scale production and distribution recently has not been on prominent display neither in Sweden at large, nor in the Uppsala region. Could it be so that an economy dominated by giant firms eventually loses its entrepreneurial qualities? Can the policy maker contribute anything beyond helping to create the institutions that define an attractive entrepreneurial climate?

The History of Pharmacia

Pharmacia was the dominant industrial player in the Uppsala regional economy for years. It was not as dominant, but still an outstanding innovator in the greater Lake Mälar regional economy around Stockholm (of which Uppsala is a part), with altogether some 2½ million inhabitants, a region that is increasingly becoming an integrated labor market.

Pharmacia has been through at least six phases of development.

I. Establishment , entrepreneurial success and *development into a pharmaceutical company;* 1911- ca 1950
II. *Innovative research phase*; the foundation for a future as a large firm is laid from the early 1950s to the late 1970s
III. *Expansion through not very successful acquisitions* during the 1980s (Under Volvo governance)
IV. Under Government governance (Procordia period 1990/91)
V. *Pharmacia as a spillover source and great technical university*- up to the Upjohn merger 1995.
VI. Attempting to commercialize its wealth of innovation through an international merger, mismanaged large scale restructuring, reconfiguration and break up ; 1995-2005

Phases I and II define the creation of Pharmacia as a large company, III through V its failed attempts to become a giant on its own and VI its break up.

Phase I: *Establishment and Development into a Pharmaceutical Company, 1911- ca 1950*

Pharmacia was founded in Stockholm in 1911 as a distributor of medical products. In 1950 it moved to Uppsala to get direct access to an advanced and innovative academic research environment. After a number of years and increasing research cooperation with Uppsala University it gradually entered a new research phase. Three product legs were developed:

1. *Salazoperin* in 1941, a combined sulpha substance and Salicylacid that was active against rheumatism and ulcerous kolis and had significantly fewer side effects than other sulpha substances.
2. The blood substitute *Dextran* in 1947 and
3. *Sephadex* in 1959 which was the dextran based substance in Pharmacia´s separation technology and the foundation of Pharmacia Biotech.

Above all, the development of the important filtering and selection technologies based on dextran that made the biotechnology industry possible began at Uppsala University in the early 1950s and may be said to be the foundation of Pharmacia as a high technology firm.

Phase II: *Innovative Research Phase*: 1950s through the late 1970s

Pharmacia began producing the artificial blood substitute *Dextran* (a winner, the brand name of which was Macrodex) in 1947 but remained a small entrepreneurial company for a long time. Dextran was the result of the successful informal cooperation with Uppsala University. Dextran was soon discovered to be a useful substance for other purposes. Products ranging from filtering techniques to ulcer treatment and skin care products are dextran based. The dextran based filtering technology was the technological base for what later became *Pharmacia Biotech*, first a division within Pharmacia then a separate subsidiary.
In fact, in the late seventies and the early 1980s Pharmacia was regarded in the US and UK venture capital communities to be, together with Danish Novo, the winning pioneers in a budding biotechnology industry, a mistaken view it turned out, as Pharmacia failed to deliver under Volvo governance (Eliasson 1997b, 2002b and below).

In 1979 Pharmacia launched the new stabilizing medium *hyaluron* acid for eye surgery (Pharmacia called the substance Healon). Hyaluron acid is a natural substance produced from the crests of cocks. It rapidly became the base for a new product line within Pharmacia. A synthetic version of hyaluron acid makes up the base for the cosmetic and medical products of Q-*Med*, a spin off from Pharmacia [10].

Phase III: *Expansion through Acquisitions- under Volvo governance; the 1980s*
The main owners of Pharmacia sold out to Volvo in the 1980s when Volvo wanted to diversify its production. Volvo had the financial resources and Pharmacia shifted gear into expansion. In 1986 it acquired both Malmö based *Leo/Ferrosan* and the Stockholm based *LKB Products,* Pharmacia´s main competitor in biotechnical separation instruments. LKB was made part of Pharmacia Biotech. LKB´s production of instruments was moved to the Pharmacia factory in Umeå that had been founded in 1967. Pharmacia, however, ran into problems under ”Volvo governance”.

Phase IV: *Under Government governance*
Pharmacia merged “anonymously” with Government owned Procordia (earlier Statsföretag) and Volvo´s food group *Provendor* in 1990 and resurfaced, merged with innovative *Kabi* in 1991 as *Kabi Pharmacia*. Kabi, in turn, had its origin in brewery business (Stockholms Bryggerier, founded in 1889) the central laboratory of which had been converted into *Kabi* in 1951 and merged with *Vitrum* (founded in 1877) into the *Kabi VitrumGroup* in 1972. Kabi was a Swedish pioneer in genetic engineering. *Kabi Gen*, the innovative part, was founded in 1978 and had developed a human growth hormone, the first genetically engineered substance in the world, cleared for use in the UK in 1985 (Frankelius 1999, p.46). When Procordia was broken up in 1993 the health care part took the name Pharmacia again (See further Östman 1994).

Phase V: Technological Spillover Source or Pharmacia as a great Technical University and Business School Combined
Already in the 1980s Pharmacia had begun spinning off “new entrepreneurial establishments”. Nilsson – Norell (1996) list 56 in the Uppsala region and 14 in Stockholm between 1985-1996. The early spin offs from Pharmacia 1984-1996 cover a wide range of

[10] The natural substance has been taken over by another Pharmacia spin-off *Bohusbiotech* (DI July 29. 2003).

technologies from technical and management consulting (*Marma Medical,* founded in 1995), investment and market introduction management (*Biolin* 1991) and product agents (*Medeca*, 1989) to biosensor instruments to measure molecular binding reactions (*Biacore* 1984), the production of (Hyaluron based) cosmetics to remove wrinkles (Q-*Med* 1987), genetic diagnostics and personalized medicine (*Eurona Medicals* 1994), dextran based infusion solutions and clinical dextran (Debrisan), for surgery and advanced ulcer treatment (*Medisan Pharmaceuticals 1994*), and the development of a technology to speed up chemical syntheses in microwave ovens (Labwell,1987),[11] diagnostic kits (*Mercodia* 1991) and a new method to make genetic tests (*ProGene* 1992). ProGene has since left Uppsala for a new location within the Lake Mälar region. Also *Radi Medical* was founded in 1988 in the pre merger period. It develops catheters to insert far into the main blood vessels for surgery, and body compatible polymers that eventually dissolve. Even though it does not use Pharmacia technology Radi Medical is staffed with Pharmacia people.

Phase VI: Post merger restructuring, break up and reconfiguration

The fragmentation and refocusing was continued after Pfizer acquired Pharmacia in 2002. Over the years Pharmacia had developed a broad based portfolio of new substances and technologies, far more than it would ever be capable of successfully developing commercially on its own. Since this fact is a critical part of the case study analysis to follow this presentation will include some detail of what was once inside old Pharmacia.

A number of Pharmacia activities had been sold off, for instance the protein substance Refacto against hemophilia to US Wyeth in 1997[12], or closed down, for instance the interesting "superprotein".

Some time during the 1980s an Italian physician discovered that an Italian family had a unique gene that produced a particular " superprotein" that was capable of cleaning the body of bad cholesterols. He patented the protein and Kabi-Pharmacia (then part of Government owned Procordia) acquired the patent in 1991. Pharmacia had begun to produce the superprotein when it merged with Upjohn in 1995. The new management closed down the project in 1996, but allowed two Pharmacia scientists to buy the patent in 1997 and start *Esperion Therapeutics* on US venture capital[13]. They had reached the stage of clinical trials in

[11] later renamed *Personal Chemistry.* Personal Chemistry merged with PyroSequencing in 2003, The new company acquired US Biotage in late 2003 and took the name *Biotage* (DI Jan. 5. 2004)

[12] *Refacto* had been developed at Pharmacia using DNA technology. This technology eliminates the risk for transfer of viruses associated with traditional blood substitutes for haemophilia extracted from human blood. A " golden egg " lost cries *Dagens Industri* (Aug. 24.1999).

2000. When Pfizer discovered the winner it was just about to lose, it bought Esperion back for US 1.3 billion (SEK 9.5 billion, DI May 4. 2004). Esperion is now part of Pfizer and located in Ann Arbor, Michigan, US

After the merger with Upjohn into PharmaciaUpjohn in 1995 most management activities, ranging from supply, R&D and marketing to the corporate headquarter (CHQ) were moved to the US. A wave of radical reorganizations was initiated including a partial withdrawal from the Uppsala region. The company began to break up and to spill technologies from its impressive research portfolio . As a consequence, however, the availability of scientifically trained and industrially experienced people in the Uppsala region increased significantly, and the rich supply of technologies and human capital still constitute its current locational advantage.

In 1997 Pharmacia Biotech (then a subsidiary company within PharmaciaUpjohn) was merged with British Amersham to be renamed Amersham Biosciences (See further Frankelius 1999). A large pharmaceutical production site in Strängnäs, the life sciences equipment supplier Pharmacia Biotech or Amersham Biosciences , Pharmacia Kabi´s nutrient broth activity, acquired by German Fresenius 1999 and *BioVitrum* (2001) a spin off from Pharmacia developing a substance for controlling obesity and an enzyme for inhibiting old age type II diabetes, were left in Sweden. The outcome of the merger with Upjohn was not much of a success.When the original Upjohn CEO had been fired a new CEO "saved the company" (BW April 26.1999). He acquired *Monsanto* in 2000, and changed the company name back to *Pharmacia Corporation*. Gradually, however, a large part of pharmaceutical research has been moved out of Uppsala. In 2002 Pharmacia Corp. spun off its agro business under the name of Monsanto. After *Pfizer* had acquired Pharmacia in 2002 it announced that it would take the company off the Stockholm Stock Exchange (*DI*, Nov. 6. 2002).

In 2004 Amersham Biosciences was acquired by General Electric´s Medical Business (DI Oct. 10 and Sv.D. Oct. 9. And 11. 2003). Currently General Electric is rapidly reorienting itself towards the markets of the New Economy (biotech and health and media and entertainment). Its new CEO was once the head of GEs Medical Systems, and is now pushing GE Healthcare in the direction of molecular medicine and medical imaging, the development of instruments to study how proteins control different cellular functions and instruments to separate and produce proteins. GEHealthcare in Uppsala has also repeated its ambitions to stay in an environment exhibiting a long tradition of biotech experience within

[13] and a very small Swedish contribution

protein research in particular and a generous supply of scientifically trained labor (BW Oct.13. 2003, Sv.D. Special Section on Biotechnology, May 13.2004, DI April 21. 2006, FT Febr. 10.2006). The ultimate announced ambition is "personalized and preventive medicine" and even though most of the technologies that came with Amersham Biosciences are vintage Pharmacia, the Pharmacia name is already beginning to fade (See BW April 26. 2004).

The New Family of Pharmacia spin offs

Active Biotech (based in Lund) was spun off in 1999. Its best selling products were all from old Pharmacia (DI Feb. 21. 2004).[14] Active Biotech is developing a pill based substance– the first in the world- against MS and targeted super antigens against cancer (See Special Section, Sv.D. May 13. 2004). Among other post merger divestments should be mentioned: *Åmic* (1998) which makes microsystems in plastics for bioapplications, *Gyros* (1998) which develops CD based micro laboratories, a technology originally developed at Pharmacia Biotech, *Visionar* (1998) which carries out contract research and *Resistentia Pharmaceuticals* which has developed an allergy vaccine that is already on its way to clinical testing. They are all based on old Pharmacia developed technologies (DN Jan.15. 2002).
By 2004 the period of restructuring, break up and reconfiguration in the Uppsala region appears to have reached a provisional conclusion. The old worry that Uppsala had lost the presence of a large scale industrial player and a competent local industrial customer is gone. Old Pharmacia and its rich portfolio of innovations are now under the governance of two US giants (Pfizer and GE), both known for their rational and effective management, and a large family of independent , new start-ups based on Pharmacia technologies and to a large extent managed by Pharmacia people, most of them within the Uppsala regional economy. The picture is however somewhat clouded. The reason Pfizer bought Pharmacia is said to be that it wanted the Cox II platform that Pharmacia got with the Monsanto acquisition, and kept, returning the rest of Monsanto to the market. The Cox II platform is however, currently a cause for concern. Merck´s Cox II based and best selling pain killer Vioxx has been shown to have serious side effects and many expect the same to be true for Pfizer´s Bextra and Celebrex (DI Febr. 16.2005 and Sv.D. Jan. 25. 2005). In addition there are doubts that Pfizer´s success strategy of the past in developing block buster drugs ("one substance fits all") will be as successful in a future world of targeted drugs and personalized medicine (BW Febr. 28. 2005). While the many small Pharmacia companies are dependent on the local

[14] Xalatan for eyes, Netrusitol for incontinence and Fragmin for blood clots

Institutional environment to commercialize their technologies, but – if successful- may become subject to a generous takeover bid of some big global company (Eliasson-Eliasson 2005), the Pfizer and GE acquisitions are already placed within the global organization of an international company with the resources needed to take winners on to industrial scale production and distribution. For them local firm performance is what matters for the local permanence of the investment.

Even though Pharmacia stock owners appear happy, others have talked about the end of a Swedish success story (DI July 16. 2002) and of a blow to the Uppsala regional economy. Some argue that "Sweden" has wasted great research for nothing (DI Feb.21. 2004). One could, of course, also argue that if that is the case, the reason must be lack of local competence to commercialize new technology, the commercialization competence being a joint responsibility of the industrial community and Government with its dominant influence on the local entrepreneurial climate. Others have argued that it takes a big company to fill in where PharmaciaUpjohn has left. Before Pfizer and GE Healthcare entered the Uppsala scene hopes to revive the Uppsala economy were pinned on the dispersed family of Pharmacia spin offs. The strongest views heard, however, were that the new firms, based on technologies released in the market from Pharmacia would take too long to become visible at the macro industrial level. There was also the purely political voices that argued that Swedish investors were better because they would honor Swedish social and labor market political ambitions, implying that they would do that at the expense of their own profitability. A positive observation in this gloom, however, was that foreign investors might contribute the complementary technology needed to commercialize the innovations and to raise local competitiveness. Here, the worry was that foreigners would pick up the technology and leave. Pfizer has been gradually closing down Pharmacia research in the Uppsala region but have chosen to stay elsewhere in Sweden. One consequence has been that the supply of scientifically trained and industrially experienced people has increased even further in the Uppsala region. There are many new start up companies in the Uppsala region that are not based on Pharmacia technologies, but that are staffed with Pharmacia people. Others have started new companies on the technology they had been party to developing within Pharmacia. Others again have taken over production and technologies that Pharmacia decided to leave, for instance *Recip* in Strängnäs. The "old" group within Pharmacia that developed the anti smoking substance Nicorette , is being reconstituted in the new company *Niconovum* (2003) to launch a competing product (DI Feb. 12. 2004). A subtle observation, however, heard in our interviews is that the "large scale" industrial management experience from

Pharmacia may not always be the right competence to run new start-up companies on meager budgets.

3. The Shake Loose Hypothesis and the Regional Policy Problem

Key to a positive version of the Shake Loose Hypothesis is that the few, perhaps only one, among the many new ventures that are real winners capable of being scaled up to a giant corporation on the basis of its innovation base, are also identified, supported and carried through the competence bloc to industrial scale production and distribution. It is still too early to tell about winners, but let us look at a few candidates that have been pointed at by experts as winners and that have also entered technologies and markets that have been said to define the future. The story to come will also explain why Pharmacia has been unable to commercialize on its own all the diverse technologies that have flowed out of its laboratories.

Pioneering Pharmacia Technologies under a Pfizerian Streamlining Regime

Biacore was founded as *Pharmacia Biosensor* in 1984 as a wholly owned subsidiary of Pharmacia. It was based on a biosensor technology project conducted jointly with the Swedish National Defense Research Institute (FOA) and the Linköping Institute of Technology. It took five years for the new company to launch its first instrument (named Biacore) in 1990, and with the exception of 2004 the company has had an uninterrupted decade of profitable years. The company is now a global leader in instruments to measure molecular binding reactions. After the Upjohn merger the company was no longer regarded as a core activity. It was introduced on the Stockholm Stock Exchange and on Nasdaq in 1996 and the name was changed to Biacore. Between 2001 and 2004 Biacore´s headquarter was moved to Switzerland (to Neuchastel) for "strategic reasons." Pfizer´s acquisition of Pharmacia in 2003, however, meant immediate change. Pfizer is known for its strict focusing on pharmaceuticals for human beings and animals and on health care. Biacore was first placed on the sales list, but buyers were again hard to find in Sweden, and were looked for in the US and the UK (*Veckans Affärer*, Nr.36. Sept. 1. 2003). Pfizer still owns more than 40 percent of Biacore. For many years Biacore had developed and manufactured unique and increasingly sensitive products for protein interaction analysis, and antibody characterization in particular that, however, required a quite large investment of its user. A new start up, Stockholm based

Attana (founded in 2002) now challenges Biacore with a less sophisticated but also less expensive product (DI Oct. 16. 2004).
Hyaluron acid, the jelly that can be used for stabilizing the eye during eye surgery, also fell outside Pfizer´s focus. The eye surgery activity was therefore sold to US *Advanced* Medical *Optics* (Sv.D., May 17.2004). Other Pharamacia pharmaceuticals for eye medication, however, do not (Sv. D. Dec.27. 2003).
Old Pharmacia and (once) *Fermenta* operated several production sites in Strängnäs (on the Lake Mälar). Some of them are still in operation, but now foreign owned, for instance DSM *Antiinfection* (Dutch owned) and *Micro Drug Development* (Swiss owned). One Pharmacia factory in Strängnäs was planning a large expansion in the production of the genetically engineered human growth hormone and substances for gerontology. This activity is now within Pfizer which has the policy to operate only one production facility of each kind. The question therefore was whether the Strängnäs facility really was a competitive alternative for that localization. The latest message (April 2006) is that Pfizer will opt for Strängnäs (DN April 11.2006. Also see Sv.D. Oct.16. 2002, Dec. 27.2003, May 31.2005, *Ny Teknik*, June 1, Nr.22. 2005).
On the whole, Pfizer´s restructuring appears not to affect Sweden as much as it affects other countries.The Swedish supply of scientific and industrial skills in the area has been quoted as the reason. However, among the four locations in Sweden of (now) Pfizer activity (Stängnäs, Helsingborg, Stockholm and Uppsala) Uppsala appears to have most activities that may be sold off because they fall outside Pfizer´s focus (Sv.D. Dec.27. 2003).

Cosmetic Innovations for Wrinkles and Incontinence

The Uppsala company Q-*Med* (1987) has developed implantats from a biosynthetic variant of the Hyaluron acid previously extracted from cocks´crests by Pharmacia and used in eye surgery. The same substance can also be used to smooth facial wrinkles because it can bind water in the skin longer than other substances. Q-Med´s substance has been cleared for use in Europe and is about to be in the US. The patent lasts through 2015. But Q-Med is also developing other uses for the hyaluron acid, for instance to inhibit incontinence. The property of the same acid to encapsulate human cells and protect them from the immune system is another project idea being developed, as is the development of a medication of diabetes based on cell therapy. *Dagens Industri* observes (Sept. 8.and Nov.25. 2003) that the stock market puts a value only on the cosmetic products and part of the cash . The ambition of Q-Med management is to become a real pharmaceutical company using the cash flow from its

successful cosmetic product line (DI May 10. 2004).

Genetically Based Diagnostics and Personalized Medicine

A method to measure allergens with antibodies (immunoglobulins) had been developed at the Bio Medical Centre (BMC) in Uppsala during the 1960s. Pharmacia took up the method and developed it into an allergy test. This was the beginning of *Pharmacia Diagnostics* (founded in 1974, as of Jan 17. 2006 renamed *Phadia)* which became the world leader in allergy testing (more below). As a consequence of Pfizer´s strict focusing of its product range *Pharmacia Diagnostics* was placed on the sales list. There was no obvious Swedish buyer (DN July 2. 2003) and no Swedish risk capitalist showed up to take on the risk. In 2004 the two British investors PPM and Triton financed a management buyout for SEK 4 billion (*Ny Teknik,* Jan.28. 2004, Nr.5). Pharmacia was also a very early pioneer in the medical technology of genetically based diagnostics and personalized medicine. It, however, eventually decided not to carry on and instead focus on the academic research markets. A group of people involved in the so called Condor Project and people from other Pharmacia projects left and started a number of companies, among them *Eurona Medicals (1994), Alfa Helix* (1990) *, Åmic* (1998)*, Melacure* (1997)*, Labwell* (1987, later renamed *Personal Chemistry*) *, Pyrosequencing* (1997) and *Radi Medical*(1988).

Eurona had developed a particular chemical testing technology using twins. The entry into Genetically based diagnostics, however, was too early for Sweden. Even though everybody is Now regarding personalized medicine as the future medical technology[15] and even though Eurona was announcing that its first product would be launched in the fall, a test that predicts which patients will respond positively to a particular blood pressure inhibitor (Sv.D. June 1999), Eurona was out of money in 1999, in the midst of a recession. The Swedish venture capital providers backed out and sold Eurona cheaply to British Gemini, which was interested in the twin testing competence only. Gemini has now been acquired by US *Sequenom*. This is exactly what should not happen during a successful transformation of a region; one of the most daring and promising ventures being shut down and/or localized out of the country. Lack of "competent and sustainable venture funding" was the quoted reason. The Swedish and UK activities have now been closed down and Sequenom is concentrating its activities to San Diego and to a German location. Some of the early patents have been returned to the previous owners who are now engaging them in a new diagnostics venture. Again, however,

[15] Cf. GE Healthcare that announces that personalized medicine is its business focus (Sv.D. Special Section on Biotech, May 13. 2004).

Swedish healthcare is not organized for efficient use of advanced diagnostics and the Swedish venture capital market is cold to this technology. Italian healthcare, however, is, and the venture is being moved to Italy, which has become the manufacturing base of *EDX Diagnostics,* based on Pharmacia developed technology. *Pyrosequencing* (1997), recently renamed *Biotage* (DI Jan. 5. 2004) is an Uppsala based firm in the biotech supply business, founded on a patent from the Royal Institute of Technology (KTH) to sequence and synthesize DNA. To begin with Pyrosequencing was run by Pharmacia people. It was, however, hit hard by the stock market downturn in 2002 and 2003, but its relatively good liquidity postition, thanks to a succesful equity issue in 2000 (DI May 14. 2002) kept it afloat. After Pyrosequencing had merged with Personal Chemistry in 2003 (DI Aug.8. 2003) top management has been changed and the strategy appears to be to grow fast through complementary strategic acquisitions, for instance the acquisition of US Biotage in October 2003. Since growth in the specialty markets of Pyrosequencing has slowed, and since the company has been working up significant losses, focusing on the winners was deemed necessary to reduce administrative overheads per sales $. With two bold acquisitions Pyrosequencing has changed both production structure and orientation towards what is believed to be high growth segments of the market (DI Oct. 15. 2003). The company has also concentrated its research to Uppsala. Biotage´s specialty is purifying molecules. It has the same end customers as the micro oven technology of Personal Chemistry, the purpose of which is to speed up organic syntheses. It was also important for the new firm to enter the markets for profitable chemical supplies. Biotage is currently looking for a company to support its old stagnating product lines based on the Pyrosequencing technology (DI Jan.5. 2004). The strategy is profitability through growth rather than through R&D.

Genetically Engineered Substances against Obesity and Type II Diabetes

The Pharmacia spin off *Biovitrum* (2001) is the largest biotech company in Sweden. It originated already in KabiVitrum (See above) where the world's first genetically engineered growth hormone was developed. Biovitrum was separated as a division within Pharmacia in 2000 that included about 400 Pharmacia researchers most of whom remained in Sweden after Pharmacia´s withdrawal. In 2002 GlaxoSmithKline took over further development of Biovitrum´s new substance against obesity and there was another one, also against obesity in the pipeline (DI Oct.24.2002, *Dagens Forskning*, Jan.7-8. 2003). Biovitrum suddenly became a new winner when it got a licencing agreement with US Amgen which will sell Biovitrum´s enzyme for inhibiting old age type II diabetes. The back side of this early licensing agreement

with a large and very competent customer firm with ample financial resources is that a larger part of profits will be allocated to the partner (DI and Sv .D. Sept. 9. 2003), a lesson that Astra (now part of AstraZeneca) once learned from its early partnership with US Merck . During the early 1980s Astra was in a similar position to that of Biovitrum, and nobody could at the time envision the discovery of Losec and its tremendous commercial success (Eliasson-Eliasson 1997). Astra struck a deal that was, and still is a winner for Merck (DI March 23. and 24. 2004). Apparently, however, Biovitrum was an interesting company that could choose among several different partners, of which Amgen offered the best deal (*Veckans Affärer*, Nov. 24. 2003. Nr 48). Despite this success it is not obvious that the company can capture such a good price that a Swedish IPO will take place anytime soon (Sv.D. Jan 2. 2004, DI April 26. 2006). Biovitrum has also decided to try to keep its projects longer and raise their value before entering into partnerships, and to build itself into a real pharmaceutical company. As a consequence it has decided to reduce its research and focus on what it has, and on the clinical development of its products. To that end it has acquired UK based *Cambridge Bio Technology* and Gothenburg based *Arexis.* The bio engineered substance against hemophilia of Biovitrum, is, however, facing intensified competition in its own backyard from Swiss owned Octapharma (*Biotech Sweden* , Oct. 25. 2005, DI Aug. 31.2005, *Ny Teknik,* June 1. 2005). The CEO of Biovitrum observes that big pharma *have to* turn to the small biotech firms to complement their portfolios of half-finished projects. The R&D budgets of the 100 largest biotech companies together still do not add up to more than the research budget of Pfizer, but, he continues, we (the small companies) get many more substances to the market (*Dagens Forskning*, Jan. 7-8. 2003). So far, however, the Biovitrum diabetes substance does not seem to be a new Losec. After new clinical tests by Amgen disappointing results are reported and the SEK 5 billion deal for a winner no longer appears a sure thing (DI April 2. 2004).

Inflammation and Autoimmune Illnesses

Malmö based *Active Biotech* acquired Pharmacia´s research company for cancer, inflammation and autoimmune illnesses in Lund 2001 (Sv.D. Jan.9. 2003) and rose on the Stockholm Stock Exchange on positive signals on its Sail MS substance. It managed a new stock issue in 2004 even though its liquidity position was very good on the policy "never wait until you really need the money. Then you are in a bad negotiating position and/or the venture capitalists have changed their minds" (DI Feb.14. and May 24. 2004). Again, a partnership with a large and probably foreign company was considered necessary to manage the financing

of clinical testing (Sv.D. Sept.17. 2003). ActiveBiotec stock rose again on positive results on both its cancer and MS substances (DI Oct. 8. 2005).

Melacure Therapeutics (1998) is another Pharmacia (Condor) based company in the drug discovery market (in Uppsala) which had focused on inflammatory disorders. It had developed a promising substance against the intestinal disorder Irritable Bowel Syndrome (IBS) for five years when the Swedish (SEB associated) venture capitalist Investor Growth Capital became impatient and forced the company into bankruptcy (2004). Another Swedish venture capitalist (Health Cap) would have liked to continue but could not do it alone. HealthCap expressed hope that the project would, nevertheless, survive even though the company had closed down (Sv.D. *Näringsliv*, March 2. 2004). Apparently Melacure´s business idea was sound and the project was picked up immediately after filing for bankruptcy.

Instruments and Protein Separation - a Lost Swedish Opportunity?

Amersham Biosciencies was the merged outcome of Pharmacia Biotech and UK Amersham Life Sciences in 1997. Already in 1996 Pharmacia Biotech management discussed a possible merger with the chemical group Perstorp (of which Perbio was a division). Perbio management saw a possibility to combine its world leading protein culture technology (which was US based) with Pharmacia Biotech´s leading protein separation technology to create a global cell culture company; a ” Swedish Solution”. Pharmacia Biotech management, however, considered Perbio too small a player and did not accept Perbio´s idea to sell off the entire, large and not very profitable instrument activity that Perbio management considered alien to a cell culture company. Perbio management balked at Pharmacia demands that current Pharmacia Biotech top management would have secure top jobs in the new company for many years. In addition, Perbio management considered instruments to be an impossible financial burden on the company that would also demand a disproportionate attention from management. Continuing the instrument business and turning it into something profitable, in fact, would demand investments on an impossible scale, and therefore be an obstacle to growth within their core market segments.

One reason for the very large investments needed in the instrument business was the rapid technological change. It was easy to stumble, lose market value and be taken over cheaply. The instruments, furthermore, did not alone generate sufficient profits. They had to be complemented with consumption chemicals. So the deal went to Amersham, which acquired Pharmacia Biotech, and Perbio went on to prosper, despite the distressed biotech industry, to

be introduced on the Stockholm stock exchange in 2000 at SEK 35 (DI Nov.8. 2000) to be acquired in 2003 for SEK 155 by US Fisher Scientific ; a ”non-Swedish solution” (DI June 27 and Aug.28. 2003).

In 2001 Amersham acquired the remaining 45 percent of Pharmacia Biotech and changed the name to Amersham Biosciences and in 2002 Amersham acquired the PET Center of Uppsala Universirty (*Ny Teknik*, Nr 20. May 15. 2002). The new company was optimistic with its dual approach and announced new recruitment to expand its protein separation activity in biotechnical substances such as insulin, and to move protein research from the UK to Uppsala just a month or so (*Ny Teknik*, Nr.35. Aug. 27. 2003) before Amersham was acquired by General Electric´s (GE´s) Medical Businesses (DI Oct. 2003, Sv.D. Oct. 9. And 11.2003) to become the core of GEHealthcare. GEH had already acquired the PET camera and the cyclotron of Swedish *Scanditech* in Stockholm (NUTEK B 1993:12, pp.159ff). The ambitions of GEH is to combine scanning (PET,MR and CT) technology and the protein technology that came with Pharmacia Biotech/ Amersham, not only to improve medical diagnostics but also to achieve early prediction and personalized remedial action, rather than costly treatment (FT Febr. 10. 2006). GEH already uses Amersham´s contrast chemicals (Sv.D. Oct. 11. 2003). GEH believes that Uppsala may become the global leader in developing protein based pharmaceuticals and after protein based pharmaceuticals comes cell therapy. To capture that new technology GEH invests SEK 1 billion in its Uppsala activity (DI April 21. 2006).

What are the consequences for Uppsala of GE´s acquisition of Amersham and the old Pharmacia Biotech? GE Health Care accounts for 42 000 of GE´s 315 000 employees. Of those 42 000 Amersham accounts for 10 000, and of them old Pharmacia Biotech for 1 500, most of them in Uppsala. What will happen to its future location? What will happen to the cell culture activity that Perbio was interested in? On this Swedish biotech guru , innovator and once Amersham board member Mathias Uhlen expresses hope: Uppsala has a “focused niche that is very profitable”. Such activities are “usually very appreciated” (DI April 8. 2004 and DN April 10. 2004). And GEH appears to have decided to stay in Uppsala for the long haul (Sv.D. April 13.2006). So old Pharmacia has certainly been replaced by two large international players with large resources and the competence to carry winners on to industrial scale production, that will greatly benefit the Uppsala economy as long as they find it attractive to stay there.

We asked in the beginning whether commercialization of new technology through big companies is more efficient than through small companies, and it certainly looks as if two

giant US corporations have created a very different biomedical future for the Uppsala economy. These players, however, have entered the Uppsala market late and made strategic choices among already created and identified winners. To be added , therefore, is that the Uppsala market is replete with supplies of such created and developed advanced biomedical products currently being industrialized within a number of small and recently founded companies. Will one, or some of them be able to become large scale winners on their own, continuing to grow through complementary strategic acquisitions from the rich local technology supplies or other sources, and will those winners be Swedish based?

4. Economic Distress or Entrepreneurship and Industrial Renaissance in Uppsala - testing for the Shake Loose Hypothesis

Testing for the positive version of the Shake Loose Hypothesis proceeds in two steps.
We *first* assess the "completeness" of the local biotech/pharmaceutical/ medical science competence bloc and come up with a preliminary conclusion.
Second, we call in some econometric evidence on the micro-to-macro development of the entire local industry in the wake of the Pharmacia break up, and compare with the same development of the same industry in the whole of Sweden.
The question was: Will the break up of Pharmacia eventually create more local prosperity than old Pharmacia would have been capable of, had it been left as it was to internally develop its wealth of technologies?

Competence Bloc Analysis
Local customer competence: Sweden at large, and the university communities in particular are well endowed with customer competence through an until recently generous health care system, and the specialties of the academic hospitals. This is clearly the case in Uppsala and the entire Lake Mälar region around Stockholm. Pharmacia, in addition served as a competent intermediate customer for the local subcontracting industry of a rich variety of technical and other services. The break up of Pharmacia, therefore, meant the disappearance of a large, competent and demanding customer to new biotech ventures. While this may have been an early concern in the mid 1990s, the emergence of the customer and management competence of Pfizer and GE should now have removed those worries. US multinationals, on

the other hand, are known for their tough demands on performance and strong inclination to shut down operations that are not up to standards. This means that the attractive features of the Uppsala regional economy will have to be maintained for this competence contribution to be sustained.

Innovative technology supplies

The break up and withdrawal of Pharmacia have meant a dramatic increase in the local supplies in the market of previously internal Pharmacia technologies and of scientifically trained and industrially experienced people. In that sense Pharmacia has raised its even previously abundant services to the local economy as a "combined technical university and business school". *Lack of innovative technology supplies*, therefore, *has not been a, and is no problem in the Uppsala regional economy.* In fact, considering the extreme variety of technologies created within the Pharmacia laboratories documented above it is unthinkable that Pharmacia would have been capable of commercializing more than a fraction of them on its own. Hence, the Shaking Loose of these locked- in resources must be considered a net contribution of entrepreneurial opportunities free of charge of Pharmacia owners to anybody sufficiently competent to take advantage of them.

Commercialization competence and entrepreneurial supply: The increase in local technology spills associated with the Pharmacia break up has meant increased business opportunities, but they have become available at a price. The willingness to start a business on these opportunities depends on the quality of the local industrial entrepreneurship base and access to industrially competent venture capital. The technologies released have been generally very advanced, normally outside the experience base of Swedish industry, and financial actors in particular, and attractive to foreign investors from economies that have more of that experience, i.e. the US and the UK. With a limited number of local entrepreneurs able and willing to bid for projects, foreign investors have been able to pick up new technologies cheaply. For local entrepreneurs/ investors this has meant more expensive opportunities and there have been complaints. Nevertheless, even though many new establishments are foreign owned talk about a deficient entrepreneurial supply is not supported by the case evidence presented above. The problem should be looked for in the next step; the local presence of industrially competent venture capitalists.

Commercialization competence: Venture capital supply

The lack of industrially competent venture capital and sophisticated financial services in Sweden compared to the US and the UK has been a negative localization factor for the new local start up companies in the wake of the Pharmacia withdrawal. Even though Sweden may figure rather favorably after the UK in Europe in industrially competent venture capital supply, both volume and variety of that supply is deficient when it comes to taking advantage of the broad flow of innovative technologies and entrepreneurship ¨released¨ in the Uppsala economy and to identify and support a sufficient number of winners to industrial scale production. Most notable is the ample supply of funds at the very early "academic" stages of new technology development, and the disappearance of funding at the early commercialization stage when resource use is increasing strongly (Eliasson 1997b, 2002b, 2005, Ch.4). The case evidence presented above also tells the story of failure of promising ventures at this critical level and of the difficulties of securing stable funding for rapid upgrading to industrial scale.[16] This is particularly so for the specialization of a large part of the Pharmacia based start ups in diagnostics, a medical technology that for some reason has not been favorably received in the Swedish venture capital community, our interviews tell. A critical pillar in the commercialization process thus appears to be deficient. The fact that many Swedish technology based companies in this and other biotech and medical areas have been picked up cheaply, and chiefly by foreign investors bears witness to the fact that the problem is to be found in the Swedish venture capital community and that Swedish venture capitalists have lost local winners .

Going industrial scale: This conclusion is further supported by the entrance in the local market of foreign industrial investors. Sweden has long been known for a disproportionately rich supply of large scale industrial management competence. The current concern, however, is whether this abundant supply is still a reality. Furthermore, the large scale industrial management competence of the past was specialized in engineering and to some extent IT, and the question is whether this competence can be generalized to biotech and related medical specialties (Eliasson 2005a, pp.404ff, 2005b). On this, however, we can observe that foreign investors have been eager to buy into several of the new companies, often outbidding Swedish investors. In addition GEHealthcare and Pfizer have acquired large parts of Pharmacia and decided to stay, citing the supply of well educated, scientifically trained and industrially experienced people in biotech and medical industries as a contributing factor to the decision to stay. This increased availability of competent people at internationally low wages has, in

[16] A comparison can here be made between the very slow commercialization of the Swedish so called Brånemark technology and the very rapid commercialization of a similar US technology, 3 instead of 17 years (Fridh 2002)

fact, become an attractive localization feature of the Uppsala region and most firms in the Uppsala region are partially staffed with people with a Pharmacia background.
Before going on to the next test stage two observations should be made. The Pharmacia breakup has released a wealth of new technologies previously locked up internally, a wealth of technologies that Pharmacia could not possibly commercialize alone. Most of these opportunities in fact cannot competently be taken advantage of in Sweden outside the Uppsala/Stockholm/Lake Mälar region. The alternatives have been foreign investors or a lost opportunity. Negative tax incentives for Swedish investors (Henreksson- Jacobsson 2003) and the lack of industrially competent local financing may, in fact, be pushing reinvestment in locally developed technology out of the country. We have already seen that many technologies have already been picked up by foreign investors. Some have been moved out of the country while for others the local supply of competent labor has been a sufficient incentive to develop the technology further locally.
In conclusion then, the competence bloc analysis should make us pessimistic about the ability of local Swedish entrepreneurs to take advantage of the technological spills from Pharmacia and fill in the vacuum left in the wake of the Pharmacia break up and withdrawal.

Industry Level Tests

First, we will present some industry statistics and econometric evidence on the development of the Uppsala biotech/pharmaceutical/medical instrument industry. Looking at Table 3 and summing up employment in the largest remaining Pharmacia employers the development between 1997 and 2004 doesn't look all that bad. This table, furthermore does not include a number of small new Pharmacia based establishments during the same period.

(Table 3 in about here)

Second, Fridh (2002) has performed two econometric tests of the positive version of the Shake Loose hypothesis i.e. of the hypothesis that the Pharmacia withdrawal from Uppsala has produced a positive total employment outcome between 1995 and up to, and including 2000. Unfortunately only employment data have been available and employment is not the interesting variable in this context. Output data would have been more interesting. Fridh reports two answers to this question. To begin with, she cannot reject the null hypothesis of a negative net outcome.
Many studies, furthermore, including that of Fridh on the health industry report that firm turnover is positively and significantly related to industrial growth. On that score we would expect positive growth dynamics to be in the works and caused by the increased turnover of

firms observed in the Uppsala region because of the Pharmacia withdrawal.
Third, while the negative effects from the withdrawal take place immediately, the timeframe of the analysis was much too short for most of the possible positive effects to show. Furthermore, many of the Pharmacia spillovers are not likely to take place in Uppsala, but in the wider Lake Mälar region. So the long- term dynamic story of Pharmacia in Uppsala is still to be told. Total production based on Pharmacia developed technologies may, therefore, still be significantly larger in the long run than if Pharmacia had continued to develop the technologies commercially on its own.

Foreign Investor Competence Bolsters Deficient Local Commercialization Performance

While the competence bloc evaluation suggested serious deficiencies at the venture capital financing stage, and perhaps also insufficient industrialization competence this pessimism was not borne out by the statistic and econometric analyses. The immediate drop in local industry development cannot be observed statistically, a number of Pharmacia activities have been moved out of the Uppsala region to the greater Lake Mälar region, and the long run positive effects in Uppsala and elsewhere are still to be seen.
So finally, a fairly positive assessment of the Uppsala situation has been made despite the lack of a complete and sufficiently varied competence bloc locally. The reason is obvious by now. The positive version of the Shake Loose Hypothesis was originally formulated in terms of an indigenous capacity of a Swedish competence bloc to fill in where Pharmacia had departed. On this, the interpretation is still in the negative. Throughout the test period, however, a number of foreign actors have invested in Pharmacia ventures and decided to stay, and after the test period Pfizer and GE healthcare have emerged on the scene. So those worrying about the absence of large scale industrial management competence in the Uppsala region do not have to worry any more, only about the continued supply of the positive localization factors that made those two companies localize to Sweden in the first place. The conclusion must, therefore, be that *the Uppsala region has tested positively for a positive version of the Shake Loose Hypothesis because sophisticated foreign investors have been attracted by the supply of technologies and found it attractive to stay* because of the rich supply of well educated and industrially experienced labor. We may therefore talk about a continued industrial renaissance in the Uppsala regional economy supported in a large measure by foreign investors.
So even though the popular press reports pessimistically that growth among the Pharmacia companies in the Uppsala region has stagnated recently (*Ny Teknik*, February 18. 2004, Nr 8)

the long-term positive effects are probably still to be seen.

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Table 1. The four mechanisms of Schumpeterian creative destruction and economic growth

1. Innovative entry
   enforces (through competition)
2. Reorganization
3. Rationalization or
4. Exit (shut down)

Source: Eliasson,Gunnar,1993, ”Företagens, institutionernas och marknadernas roll i Sverige”, Appendix 6 in A. Lindbeck (ed.), *Nya villkor för ekonomi och politik* (SOU 1993:16) and G. Eliasson (1996). *Firm Objectives, Controls and Organization – the use of information and the transfer of knowledge within the firm*. Boston/Dordrecht/London: Kluwer Academic Publishers, p. 45.

Table 2A. The dominant selection problem

Error Type I: Losers kept too long

Error Type II: Winners lost

Source: G. Eliasson – Å. Eliasson, 1996. ”The Biotechnological Competence Bloc”. *Revue d’Economie Industrielle*, 78-4^{0}, Trimestre.

Table 2B. Actors in the competence bloc

1. Competent and active *customers*
2. *Innovators* who integrate technologies in new ways
3. *Entrepreneurs* who identify profitable innovations
4. *Competent venture capitalists* who recognize and finance the entrepreneurs
5. *Exit markets* that facilitate ownership change
6. *Industrialists* who take successful innovations to industrial scale production

Source: G. Eliasson – Å. Eliasson, 1996. ”The Biotechnological Competence Bloc”, *Revue d’Economie Industrielle*, 78-4^{0}, Trimestre.

Table 3: **Employment in Pharmacia and some Pharmacia spin-off companies in Uppsala 1997-2004**

	1997	200	2002	2004
Amersham Biosciencies (Now GE)	750	760	950	1000
Biacore	70	120	180	185
Biovitrum			75	90
Fresenius Kabi		450	850	600
Pharmacia	1 695	1 397	1 250	-
Pfizer				900
Pharmacia Diagnostics				550
Total	2 516	2 743	3 385	3 400

Source: *Ny Teknik*, Febr.18. 2004, No.8