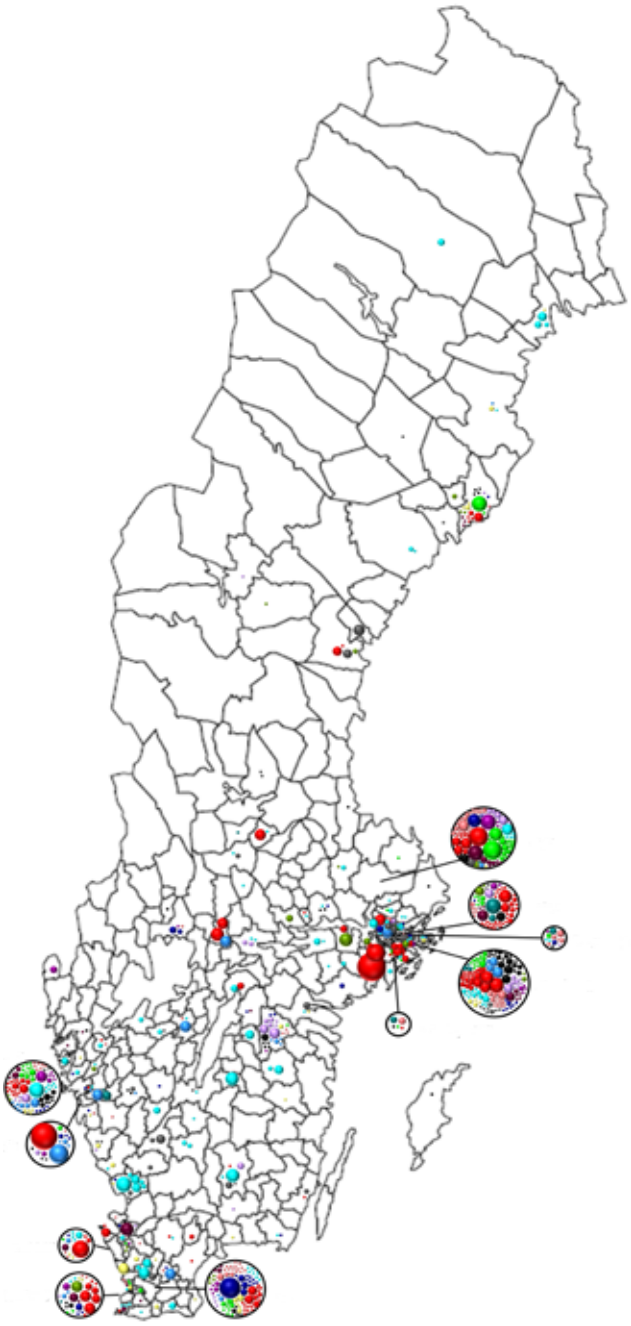
VINNOVA ANALYSIS
VA 2014:03

Global trends with local effects

The Swedish Life Science Industry 1998-2012

Anna Sandström



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VINNOVA - develops Sweden´s innovation capacity for sustainable growth

VINNOVA is Sweden's innovation agency. Our mission is to promote sustainable growth by improving the conditions for innovation, as well as funding needs-driven research.

VINNOVA's vision is for Sweden to be a world-leading country in research and innovation, an attractive place in which to invest and conduct business. We promote collaborations between companies, universities, research institutes and the public sector. We do this by stimulating a greater use of research, by making long-term investment in strong research and innovation milieus and by developing catalytic meeting places. VINNOVA's activities also focus on strengthening international cooperation. In order to increase our impact, we are also dedicated to interacting with other research financiers and innovation-promoting organisations. Every year VINNOVA invests about SEK 2.5 billion in various initiatives.

VINNOVA is a Swedish government agency working under the Ministry of Enterprise, Energy and Communications and acts as the national contact agency for the EU Framework Programme for R&D. We are also the Swedish government's expert agency within the field of innovation policy. VINNOVA was founded in January 2001. About 200 people work here and we have offices in Stockholm and Brussels. Our Director General is Charlotte Brogren.

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Global trends with local effects

The Swedish Life Science Industry 1998-2012

ANNA SANDSTRÖM

Content

Preface

Operations at VINNOVA – the Swedish innovation agency – require a solid knowledge of the Swedish national, regional and sectorial systems for innovation in an international perspective. This includes knowledge of the stakeholders in the innovation system as well as their respective roles, global context, networks and innovation processes. The knowledge base is used in strategy processes, in dialogues with stakeholders in the innovation system, in operative activities and as a support during follow-up, evaluation and effect analyses of VINNOVA activities.

The following components are part of the knowledge needed about innovation systems. These affect the ability for innovation, and therefore Swedish competitiveness:

- The economy and industrial trends
- Policies and systems
- Research, development and innovation
- The needs and challenges of society

Within its framework of strategic monitoring VINNOVA has embarked on a series of analyses of trends for several branches of industry. Parameters examined include business structure, strategic areas for renewal and cooperation in research, and innovation. On-going or recently completed studies include: Life Science, Automotive; Chemicals; Mines and minerals; Metals; Maritime; Pulp and paper; Information and communications technology; Environmental Technology, Energy and finally, Consultancies. The studies are conducted using the same overall methodology, but with certain adaptations to suit the specific characteristics of each branch. VINNOVA intends to supplement these studies with analyses of other branches of industry as well as additional aspects of the innovation systems while taking an international context into consideration. Furthermore these studies will be updated in order to reveal trends, renewals and structural alterations. The present study analyses businesses in the Life Science industry.

The present report has been based on previous studies of the Life Science industry. The work has been carried out in close co-operation with stakeholders in the innovation system and during the process several interviews have been carried out in order to complement the empirical data. The processes and their results are an important part of the VINNOVA dialogue with the regions and the value VINNOVA can offer back to them. The factual material is intended for use in strategic discussions by various stakeholders and stakeholder clusters. In addition to the reports, it is intended to create databases of the collected information, as well as a graphic interface for the presentation of results from the database. This, in turn, will enable the creation of presentations that can be adapted for different contexts and intentions.

The study has been carried out by Anna Sandström, VINNOVA and the consultant companies Addendi and Okatima. VINNOVA process manager were Göran Andersson.

VINNOVA in March 2014

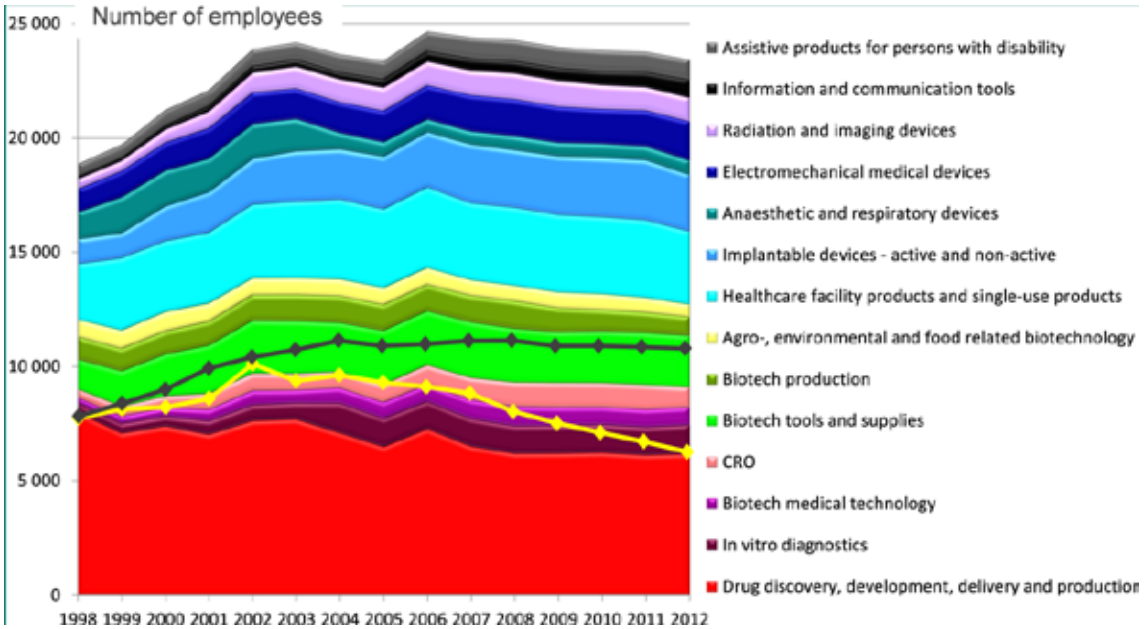
Jenni Nordborg
Head of Bioentrepreneurship Department
Health Division

Göran Andersson
Programme Manager
Transport & Environment Division

Short facts

ISSUE AND SWEDISH TOTAL	LIFE SCIENCE RESULT	COMPARISON
Total life science industry	40 764 employees in 1 487 companies	
Employment excluding sales and marketing	29 652 employees in 791 companies	Employment three times higher in automotive and over 130 000 in ICT
Public R&D spending at universities [total: SEK 29.7bn]	Medicine and biotechnology: 30 percent	Engineering: 23 percent
R&D investments by Swedish industry [total: SEK 81.1bn]	SEK 7.8bn, i.e. 10 percent of total (pharmaceuticals industry)	Automotive industry 19 percent; Computers, electronics and optics 23 percent
R&D investments in relation to net turnover	11.6 percent of net turnover invested in R&D (pharmaceutical industry)	Automotive industry 5.5 percent; computers, electronics and optics 13.6 percent
PhDs employed in Swedish industry [total: 6 498]	1 135 or 18 percent, of PhDs employed by Swedish industry (pharmaceutical industry)	Automotive industry 12 percent; computers, electronics and optics 2 percent
Share which are R&D personnel [not only PhDs, 61 224 in total]	35.4 percent of the employees are R&D personnel (pharmaceutical industry)	Automotive industry 12.4 percent; computers, electronics and optics 32.4 percent
Export [total: SEK 1 170bn]	7.7 percent of total export by Swedish industry (pharmaceuticals 4.9 and medical technology 2.8, biotechnology not available)	Automotive 10.8 percent; telecom, radio and TV appliances 10.4 percent

The number of employees in the business segments of the Swedish life science industry over time; all sales and marketing companies (dark line) and AstraZeneca (yellow line) 1998-2012 (40 764 employees in total 2012, i.e. sum of lines and surfaces)



Sammanfattning

Innovation är av avgörande betydelse för ekonomisk utveckling och konkurrenskraft. Analyser av innovationssystem ger möjligheter att förstå vilka villkor som främjar, hindrar eller utgör förutsättningar för framgångsrika innovationsprocesser. Kunskapen innebär en bas för att forma åtgärder med syfte att förbättra innovationssystemet så att det bättre främjar konkurrenskraft, attraktivitet och ekonomisk utveckling.

Både i länder med en lång tradition av omfattande kommersiell verksamhet inom Life Science och i länder där verksamheten är relativt ung, anses industrin ha stor potential att bidra till långsiktig ekonomisk utveckling men också leda till positiva samhällseffekter. Life Science företagen i Sverige utgör idag ett segment i svenskt näringsliv med stor ekonomisk betydelse som har en stark koppling till offentliga investeringar i forskning och utveckling men också till politiska beslut.

Life Science företagens produkter och tjänster möter medicinska behov och bidrar till ökad hälsa och livskvalitet. Utvecklingen inom bioteknik ger även en ökad kunskap om livets minsta beståndsdelar och processer. Genom att använda naturens egna lösningar kan effektivare produktionsprocesser, nya material med skräddarsydda karaktäristika liksom sensorer som används i många branscher eller i miljötekniska lösningar utvecklas. Kunderna kan t.ex. finnas i kemi-, livsmedels- eller massa- och pappersindustrin liksom inom miljöteknik eller i hälso- och sjukvårdssystemet. I denna studie inkluderas de företag som har huvudfokus inom Life Science och studien analyserar inte andra delar av, eller funktioner i, innovationssystemet. Översikten presenterar olika aspekter av Life Science industrin och baseras på en databas skapad och kategoriserad av VINNOVA. Tidsperioden som studeras är åren 1998-2012.

År 2012 omfattade industrin 1 487 företag med 40 764 anställda i Sverige. Många av företagen har en större del av sin verksamhet utanför Sverige. Av dessa är antalet företag inom forskning och utveckling (FoU), konsultverksamhet eller produktion 791 med 29 652 anställda, dvs. exklusive företag med fokus på försäljning och marknadsföring. Företagen inom försäljning och marknadsföring, som också ofta driver kliniska prövningar i Sverige var 696 med 11 113 anställda.

Om vi jämför antalet anställda i företag inom Life Science med andra näringsgrenar som analyserats med samma metodologi (där företag inom försäljning och marknadsföring inte räknas in) så framgår det att något färre personer är anställda i gruv- och mineralindustrin, medan något fler verkar inom kemiindustrin, företag inom den maritima näringen, eller i metallindustrin. Företag inom energiområdet respektive miljöteknik har ungefär dubbelt så många anställda och fordonsindustrin är tre gånger så stor medan IKT-företagen med sina 130 000 anställda, är 4,4 gånger större än Life Science industrin. Life Science företagen är mycket forsknings- och exportintensiva i relation till antal anställda.

Life Science industrin växte i antal anställda i början av den studerade perioden och kulminerade 2006 med över 45 700 anställda. Den senaste femårsperioden har industrin minskat med drygt 4 000 anställda varav drygt 2 200 sedan 2009. AstraZeneca har minskat antalet anställda i Sverige med 1 800 under hela perioden och minskningen har omfattat nästan 3 200

den senaste femårsperioden. Nedläggningen av FoU-enheten i Södertälje har inte slagit igenom fullt ut i statistiken för AstraZeneca 2012. AstraZenecas neddragningar har drabbat ett flertal länder och är en del av en trend inom de största globala läkemedelsförtagen avseende försäljning (hädanefter kallade ”Big Pharma”).

Om man exkluderar AstraZeneca och företagen inom försäljning och marknadsföring så har antalet anställda varit konstant för företag och koncerner med mer än 250 anställda i Sverige under den senaste femårsperioden. För mikro-, små och medelstora företag var utvecklingen mycket positiv fram till 2007 och har sedan dess planat ut för att sedan minska något. Utvecklingen för dessa motsvarar en total ökning av antalet anställda med 60 procent eller ungefär 3 550 anställda. Under den senaste treårsperioden minskade dock sysselsättningen hos de mikro-, små och medelstora företagen med 760 anställda. Även företagen inom försäljning och marknadsföring växte i början av perioden, men sedan 2004 har antalet anställda varit i det närmaste konstant. Vid sidan om AstraZenecas nedskärningar samt exklusive marknadsbolagen har industrin minskat med 990 anställda senaste femårsperioden varav 560 den senaste treårsperioden. Ett fåtal nedlagda större verksamheter står för lejonparten av denna minskning.

Tio av de fjorton delområden av Life Science industrin som inkluderats i föreliggande analys har ökat antalet anställda sedan 1998. ’Implantat’, ’Biotekniska verktyg’ och ’In -vitro diagnostik’ har ökat mest. Under den senaste treårsperioden har fem segment ökat antalet anställda: ’Informations- och kommunikationsverktyg’, ’In-vitro diagnostik’, ’Biotekniska verktyg’, ’Utrustning för anestesi och respiration’, ’Elektromekanisk medicinsk utrustning’. Det mesta av utvecklingen inom industriell, agro-, livsmedels- och miljöbioteknik sker, som tidigare nämnts, i stora företag som inte inkluderas i denna studie. Det finns dock exempel på framgångsrika intermediära företag som kommersialiserar den ökade kunskapen även inom dessa fält.

Antalet företag med ett utländskt moderbolag har ökat och takten på utländska förvärv ökade efter 2003. Totalt identifierades 108 utlandsägda företag 2012 (exklusive företagen inom försäljning och marknadsföring), dvs. 14 procent av företagen. Ungefär 61 procent av de anställda verkar i utlandsägda företag. Det finns ett fåtal exempel på att uppköp har lett till att verksamheten i Sverige lagts ner men fler av förvärven har lett till fortsatt och ofta även ökad verksamhet i Sverige.

De dominerande Life Science regionerna i Sverige är: Stockholm, Uppsala och Södermanland (50 procent av de anställda); Västra Götaland och Halland (20 procent); Skåne (16 procent). I relation till befolkningen har Uppsala län störst andel, med över två procent av befolkningen i åldern 16-64 anställda i företag inom Life Science och sedan följer Stockholms län, regionerna Skåne respektive Västra Götaland. Utanför branschsegmentet läkemedelsutveckling (som domineras av AstraZeneca) har antalet anställda växt i regionen Stockholm, Uppsala och Södermanland. Tillväxten har dock varit störst för regionen Västra Götaland och Halland, en ökning med mer än 3 200 anställda. Skåne har ungefär lika många anställda 2012 som 1998 trots nedläggningen av AstraZenecas FoU-enhet i Lund då ett antal andra företag har haft en mycket positiv utveckling. Under den senaste tre-årsperioden har dock sysselsättningen i Skåne minskat stort medan tillväxten har fortsatt i Västra Götaland och Halland. Vid sidan om den omfattande minskningen inom läkemedelsutveckling i Stockholm, Uppsala och Södermanland, har även industrin i övrigt minskat något.

Inom medicinteknik ökade varuexporten fram till 2009 då tillväxten planade ut. Efter en lång periods uppgång har exporten minskat för läkemedel sedan 2009. Bioteknikområdet är inte möjligt att fånga i den offentliga handelsstatistiken.

Antalet företag med mindre än 50 anställda har minskat de senaste åren efter en lång periods uppgång, det gäller särskilt företag med mindre än tio anställda. En av flera möjliga orsaker är bristande tillgång på finansiering för tidiga faser fram till att kommersiella aktörer som riskkapitalbolag eller resursstarka partners bidrar till finansieringen av innovationsprocessen. Fler innovationsprojekt drivs också längre virtuellt innan ett företag startas. För offentliga aktörer blir det viktigt att incitamentstrukturen inte främjar för tidig start av företag innan tillräcklig teknisk och affärsmässig verifiering. En orsak till minskningen är också ett antal fusioner och förvärv liksom att ett fåtal förtetag har vuxit till fler än 50 anställda.

Svenska aktörer har en lång tradition av att framgångsrikt ta innovationer inom Life Science ut på världsmarknaden. En historik med platta organisationer, excellent forskning, ett innovationsvänligt hälso- och sjukvårdssystem, förmåga till tvärvetenskaplig samverkan liksom samverkan mellan olika sektorer i samhället har lett till ett kreativt klimat för de iterativa, evolutionära innovationsprocesserna inom Life Science. Den gängse bilden av att de mogna företagen (ofta med utländsk koncernmoder) behåller sin närvaro i Sverige har på senare tid utmanats av ett antal beslut om att lägga ner både FoU- och produktionsenheter. För att åstadkomma en positiv utveckling behöver närvaron i Sverige ge ett kontinuerligt bidrag till koncernens innovationsprocesser och konkurrenskraft. Det sker bl.a. genom att tillvarata ett samarbetsvänligt svenskt klimat i ett ekosystem med relevanta aktörer såsom offentliga aktörer, leverantörer, akademi och hälso- och sjukvården liksom dessa organisationers internationella nätverk. Excellens inom forskning samt incitament för vårdpersonal att forska och samverka med företag är exempel på faktorer som bidrar till attraktivitet. Dessa företag har en global närvaro och det finns många attraktiva alternativ avseende var deras investeringar och FoU lokaliseras. Det finns en reell risk att de finner mer attraktiva miljöer i andra länder, som också står för större marknadsandelar. Förankringen av de framgångsrika företagen till svenska forsknings- och innovationsmiljöer är således av stor vikt. För att nya produkter som används i hälso- och sjukvården ska nå marknaden krävs att hälso- och sjukvårdssystemet är både en aktiv kund som tydliggör de behov som finns och en aktiv partner i innovationsprocessen. Detta gäller under hela produktens livscykel, t.ex. även för att utvärdera alternativa behandlingar.

Vissa branschsegment inom medicinteknik domineras i ökande uträckning av ett fåtal globala företag som i det närmaste formar oligopolmarknader. En konsolidering pågår och små innovativa företag blir i ökande utsträckning intermediärer som licensierar produkter och tjänster till de stora koncernerna, är partners i deras innovationsprocesser eller blir uppköpta när de är framgångsrika.

Läkemedelsindustrin fokuserar på att minska riskerna, kostnaderna och utvecklingstiderna i innovationsprocesserna. Detta har exempelvis lett till att små och stora företag liksom finansiärer alltmer fokuserar på redan utvärderade aktiva substanser för nya indikationer och med ny formulering samt kombinationsläkemedel. Det har också lett till ett ökat fokus på särläkemedel. Det finns exempel på små svenska företag som framgångsrikt har tagit nya läkemedel till marknaden eller till en lönsam exit inom dessa områden. Samtidigt utvecklas i Sverige nya verktyg för radikal innovation, t.ex. för validering av nya målmolekyler som läkemedel sedan ska riktas mot liksom verktyg för effektivare identifiering och utvärdering av läkemedelskandidater. Det som kallas ”companion diagnostics”, dvs. att använda biomarkörer

och/eller genetiska tester för att identifiera patientpopulationer med önskvärt svar på en viss behandling, får ökat utrymme, vilket också är ett område med potential för svenska aktörer att utveckla innovationer inom.

De små innovativa företagen som ofta är akademiavknoppningar står inför många, och ofta ökande, utmaningar på sin väg att ta nya lösningar till marknaden:

- Regulatoriska krav
- Hälsoekonomisk dokumentation
- Förståelse för, och hantering av, hälso- och sjukvårdssystemens processer
- Marknader dominerade av oligopol
- Resurser, nätverk och kompetens för att nå ut på internationella marknader och få in sina produkter i de ersättningsmodeller som finns

Den radikala omstruktureringen av Big Pharma företagen har lett till en drastisk minskning av deras interna FoU vilket frigör resurser för externa investeringar. De avser att i ökad utsträckning lita till externa partnerskap, licensiering och uppköp. Många länder sjösätter initiativ och genomför organisatoriska förändringar för att bli mer attraktiva för framtida investeringar. I till exempel Storbritannien har ett antal åtgärder vidtagits såsom exempelvis systemförändringar i hälso- och sjukvården, införande av kopplingar mellan företagsbeskattning och patentering, program för små- och medelstora företag, investeringar i strategiska forskningsområden och nya former av ’centres of excellence’.

Sammantaget lyckas för närvarande inte den positiva utvecklingen i delar av life science industrin motverka nedskärningarna hos ett fåtal större företag, särskilt AstraZeneca. Den globala och därmed också den svenska omstruktureringen av Life Science industrin och andra förändringar i innovationssystemen och innovationsprocesserna innebär också en utmaning för beslutsfattare i de offentliga delarna av innovationssystemet. Offentliga aktörer söker förse systemets aktörer med relevanta incitament, stöd och finansiering för att främja en framgångsrik utveckling av nya och etablerade verksamheter. Aspekter som diskuteras är exempelvis: Hur svenska miljöer kan bidra till förnyelse och förankring av etablerade företag. Hur framväxten av attraktiva forsknings- och innovationsmiljöer kan stödjas. Hur aktörer kan tillgodogöra sig den information och kunskap som krävs för professionell rådgivning till entreprenörer. Hur processerna som väljer vilka initiativ och projekt som ska stödjas ska se ut samt vilka underlag som krävs för att fatta dessa beslut.

Summary

Innovation is fundamental to economic development and competitiveness. Analysis of different innovation systems makes it possible to understand what conditions underlie, enhance, or impede innovation and how these conditions differ from system to system. This leads to a firmer basis for measures by which the present innovation system may be stimulated to bring about better competitiveness, attractiveness and economic development.

In many countries today, life science is considered a critical foundation of long-term economic development, as well as having positive societal effects. The life science industry is an important segment, with economic and political significance for today's society in Sweden. It also contributes to health and wellbeing through innovative solutions that meet medical needs. In addition, biotechnological inventions contribute to increased knowledge about the mechanisms behind the fundamental biological life processes. By using nature's own solutions, it is possible to achieve results such as more effective production processes and new materials with tailor-made characteristics, as well as sensors used in many branches of industry or for environmental technology solutions. Customers for these applications can, for instance, be found in Swedish staple industries such as pulp and paper, food, agriculture, and chemicals, as well as in the field of environmental technology and healthcare provision. However: only companies with life sciences as their core activity or majority business are included in the present analysis. The present study focuses on companies but does not account for other parts of, or functions in, the innovation system. The overview presents different aspects of the Swedish life science industry and is based on the life science company database created and categorised by VINNOVA. The studied time period is1998-2012.

In 2012, the industry in Sweden encompassed 40 764 employees in 1 487 companies. Many of the companies have larger operations in other countries but only their activities in Sweden are included. The number of companies in Sweden active in research and development, product development, consulting or manufacturing (i.e. excluding sales and marketing) within the included business segments was 791, with a total of 29 652 employees. Companies dedicated to sales and marketing, often also managing clinical trials in the region, employed 11 113 personnel in 696 companies.

If we compare the number of employees to the results from similar analyses of other industries we see that there are slightly fewer employees in the mining and minerals industry and slightly more employed in the chemical, maritime and metals industries than in the life science industry. The energy and clean tech industries are more than twice as big, automotive three times larger and the ICT-industry has more than 130 000 employees. The life science industry is very export and R&D-intensive in relation to its employment in comparison to other industries.

The life science industry grew during the first half of the studied time period and peaked in 2006 with over 45 700 employees. In the latest three-year period the industry has declined by more than 2 200 employees and by approximately 4 000 since 2007. AstraZeneca has declined by over 1800 employees over the entire time period and by almost 3 200 in the latest five-year period. However the impact of closing the Södertälje R&D site was not fully expressed in the figures for 2012. The steep decline in employment by AstraZeneca has also affected other

countries and is part of a trend among the largest pharmaceutical companies in terms of sales (henceforth referred to as 'Big Pharma').

Excluding AstraZeneca and companies in sales and marketing, employment has been constant in the large companies and corporate groups (>250 employees) in the latest five-year period. The employment levels among the micro-, small- and medium-sized companies increased until 2007 and then levelled off followed by a slight decrease; in total an increase of almost 60 percent or about 3 550 employees. There has however been a decline in the latest three-year period by about 760 employees. Also, the sales and marketing companies in Sweden grew in the beginning of the studied period. The employment in those companies has been almost constant since 2004. Excluding AstraZeneca and companies in sales and marketing, employment has in total declined by 990 in the latest five-year period and by 560 since 2009. A few discontinued, larger operations are responsible for most of this decline.

Ten out of the 14 business segments included in the life science industry have increased their employment since 1998. 'implantable devices', 'biotech tools' and 'in-vitro diagnostics' have grown the most. In the latest three-year period, five business segments have grown:

- Information and communication tools
- In vitro diagnostics
- Biotech tools and supplies
- Anaesthetic and respiratory devices
- Electromechanical medical devices

Most of the development of innovative products in the industrial, agro-, food and environmental biotechnology area is done in large companies not included in the present analysis. There are, however, a few examples of intermediary companies included in the analysis that have successfully commercialised the increased knowledge in the field.

The number of companies (excluding the companies in sales and marketing) with a foreign parent company has increased over time, a trend gaining pace since 2003. In total, 108 companies were identified as having a foreign parent company in 2012, i.e. 14 percent of the companies. About 61 percent of the employees in the life science industry are working in companies with a foreign parent company. A few foreign acquisitions have led to the closing of the Swedish operations. More acquisitions have led to continued and often increased operations in Sweden.

The dominating life science regions in Sweden in 2012 were:

- Stockholm, Uppsala and Södermanland (50 percent of employment),
- Västra Götaland and Halland (20 percent),
- Skåne (16 percent).

In relation to population aged 16-64, Uppsala had the highest density, with over 2 percent of the population employed in the life science industry; Stockholm, Skåne and Västra Götaland follow on. Outside of the drugs segment (which is dominated by AstraZeneca), the number of employees has grown in the Stockholm, Uppsala and Södermanland region. However, the steepest growth in employment is seen in the Västra Götaland and Halland region. The development in Skåne has been almost flat 1998-2012 despite the closing of the AstraZeneca unit, since a number of other companies have shown a very positive development. In the latest

three-year period however, the employment in Skåne has declined steeply and continued to grow in the Västra Götaland and Halland region.

For medical technology products exports grew until 2009, at which point development levelled off. For pharmaceuticals there has been a decline since 2009, after a long period of growth. It is not possible to trace the trade in biotechnology products in the same manner as pharmaceuticals and medical technology.

The number of micro- and small-sized companies has decreased after a long period of growth. This is especially the case for micro-sized companies. Plausible explanations include that it has become more difficult to finance the early stages until commercial actors such as venture capital or resource-rich partners and customers start contributing to the financing of new ventures. More projects are also run virtually, using outsourcing and networking in the innovation process for a longer period before starting a company. For public actors it becomes important not to incentivise the too early formation of companies, before enough technical and business verification is in place. A number of mergers and acquisitions in the Swedish life science industry have also reduced the number of micro- and small-sized companies.

Swedish actors have had a long tradition of successfully bringing radical life science innovations to world-wide markets. Flat, non-hierarchical organisations, excellent research, an innovation-friendly healthcare system and traditions of multi-disciplinary collaboration between different sectors in society have generated a creative climate for the iterative, evolutionary life science innovation processes. The image of the mature companies (often with a foreign parent company) maintaining their presence in Sweden has, however, been challenged in recent years by a number of decisions to close both Swedish manufacturing and R&D operations.

In order to achieve a positive trend, the Swedish presence needs to be seen as continuously contributing to the companies' innovations and competitiveness, drawing on a collaborative climate in an eco-system of relevant actors such as suppliers, academia and the health service, as well as their international networks. To be an attractive milieu for collaboration, excellence in science and incentives for clinicians to do research and collaborate with industry is needed. These companies have a global presence and there are several attractive alternatives regarding where their R&D is to be located. Thus, there is a real risk that they find more competitive milieus in other countries, which also represent larger markets. The anchoring of these prosperous companies to Swedish research and innovation milieus thus becomes important.

The healthcare system needs to be both an active customer, making the needs of the healthcare system clear to the industry, and an active partner in the innovation process for new inventions to enter the market. This applies throughout the product life cycle, for instance to monitor the outcomes of alternative treatments.

Most of the business segments in medical technology are becoming increasingly dominated by a few multinational corporations forming oligopolistic markets. Consolidation is ongoing and the small, innovative companies are increasingly tending to become intermediaries licensing inventions to the large corporations, being partners in their innovation process or being acquired when they are successful.

The pharmaceutical industry is focused on reducing the risks, costs and development time in the innovation process. This has led to small firms, large companies and investors all having an increased focus on the use of already evaluated, and used active substances for new indications

and in other formulations and combinatory drugs. There is also an increased pipeline in orphan drugs. In these fields, there have been a few examples of very small Swedish companies successfully bringing drug candidates to the market or to a profitable exit. At the same time, new tools for radical innovation are being developed in the Swedish innovation system, for example inventions and services aiding the evaluation of new targets, as well as the identification and validation of candidate drugs. Companion diagnostics with the use of biomarkers or genetic diagnostics is also being increasingly utilised around the world; this is also an area with potential for innovations from Swedish actors.

For the small, innovative firms, often academic spin-offs, the challenges to the process of bringing inventions to the market are stiff. These challenges include:

- increasing regulatory demands,
- the need for health economics documentation,
- cost containment procedures in health services,
- oligopolies already having large market shares,
- obtaining the resources, knowledge and network needed to reach out to global markets and get the products reimbursed.

The restructuring of Big Pharma companies has led to a drastic downsizing of their in-house R&D, increasing the funds available for external investments. They intend to increasingly rely on external partnering, licensing and acquisitions. Many countries are launching initiatives and changing organisational structures on the system level to make their life science innovation system more attractive for future investments. For instance, the examples from Great Britain are manifold, with systemic changes in the healthcare system, the patent box, SME programmes, investments in strategic areas and new centres of excellence being launched and organised in new ways.

The positive trends in some parts of the Swedish life science industry are currently failing to counteract the decline in a few large companies; AstraZeneca in particular. The global and Swedish restructuring of the industry described above and other changes in the innovation system and innovation processes has led to a stiff challenge for the public part of the innovation system. This part aims to provide the system with appropriate incentives, support and financing to benefit the prosperous development of old and new ventures. The changing conditions in global innovation processes raise a number of discussion points. These include (but are not limited to): how can we support continuous renewal of mature companies and their anchoring in Sweden? How can the development of attractive research and innovation milieus be supported? How can actors in the system accumulate the necessary knowledge to provide professional advice to those embarking on new ventures? How should we design the process by which we select what ventures to support? What knowledge is needed as input to the selection?

1 Introduction

Innovation plays a pivotal role in creating economic growth and a competitive society. Analysis of different innovation systems makes it possible to understand what conditions underlie, enhance, or impede innovation and growth and how these conditions differ from system to system. This leads to a firmer basis for measures by which the present innovation system may be stimulated to bring about better competitiveness, attractiveness and increased growth.

In many countries today, life science is considered a critical foundation of long-term innovation and growth in industry, as well as having positive societal effects. The life science industry is an important segment, with economic and political significance for today's society in Sweden. It also contributes to health and wellbeing through innovative solutions that meet medical needs. The health care sector can benefit from new drugs, faster, earlier and better diagnostic tools, new medical devices and e-health solutions, individually based treatments with better efficiency and fewer side effects, regenerative medicine, gene therapy and the use of new bio- and biocompatible materials. There is also a demand for innovative preventive care solutions.

In addition, biotechnological inventions contribute to increased knowledge about the mechanisms behind the fundamental biological life processes. By using nature's own solutions, it is possible to achieve results such as more effective production processes and new materials with tailor-made characteristics, as well as sensors used in many branches of industry or for environmental technology solutions.

The growth potential include the knowledge and research intensive life science companies that lead the development, often in close collaboration with scientists at the universities. It also includes the subcontractors, production facilities, and collaborative partners of these enterprises. The potential for renewal is also large for the consumers of the knowledge and expertise that is accumulated and the services and products that are being developed. Customers for these applications can, for instance, be found in Swedish staple industries such as pulp and paper, food, agriculture, and chemicals, as well as in the field of environmental technology and healthcare provision.

The smaller life science companies are often intermediaries, i.e. suppliers of technology platforms, knowledge, services, and product embryos to larger companies, such as international pharmaceutical and medical technology companies or large companies in the food sector. The products they sell or licence can for example be drug candidates, software solutions or micro-organisms which have a beneficial influence on health and therefore can be used in functional food. Products can be the licensing of patented results. Many companies also develop products and take them to the market themselves. The companies often form strong networks with: their customers; academia; the health service and other relevant organisations in the innovation system. In these networks knowledge is exchanged and thus the companies gain insight into frontline research and the needs of their costumers whereas academia get insights into industrial innovation processes and the issues industry deals with on the road to launching new products

and services on the market. More and more of the innovation processes are also outsourced to niched service companies. They contribute specialised services in different phases of the most often iterative processes.

The life science industry is undergoing a major restructuring on a global scale. Accurate knowledge of the extent, structure and development of this industry, combined with information about international industrial, scientific trends and needs of society, is essential for sound policy decisions.

The present study focuses on companies but does not account for other parts of the innovation system such as the healthcare sector, public authorities, universities or other research organisations which are important players in the life science innovation system. Some of the technologies used by the life science industry are also used by other sectors such as the forest, pulp and paper industry and the food industry but these are not included in the study. Only companies focusing on the business segments described in the next chapter are analysed.

The overview presents different aspects of the Swedish life science industry and is based on the life science company database created and categorised by VINNOVA. The official NACE categories (statistical categories usually used to classify companies by industry) cannot easily be used for life science companies, as they are scattered among many NACE categories. Thus, NACE categories have been used to identify some of the relevant companies and have been combined with other sources of information to obtain the total company population in the present study. It should be noted that there is a delay between registering a new company and that company submitting its first annual report to the Swedish Companies Registration Office. Also, other changes due to mergers, acquisitions and liquidations appear with some delay in the statistics.

The companies have been classified into different sectors, business segments and core activities. The sectors are defined as the medical technology sector, the biotechnology sector and the pharmaceutical sector and the companies are also further divided into business segments. The companies' activities are categorised under the following headings: sales and marketing, manufacturing, consultancy, incremental product development and exploratory research and development (R&D). The methodology will be described further in the following chapter.

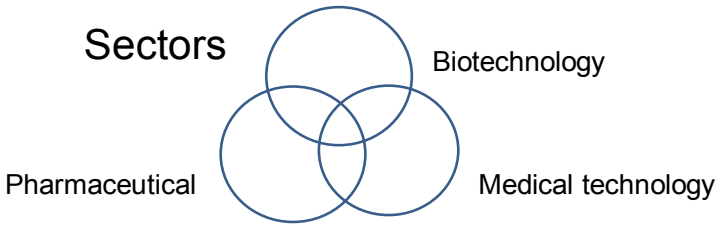
The present analysis of the life science industry includes exports, geographical location, employment, results after financial items, parent company nationality, participation in the EU seventh framework programme as well as the balance in trade in goods for pharmaceuticals and medical technology. The visualisation is based on the distribution of individual companies according to the size of the companies in terms of employees, export, business segments and activities. This gives a snapshot of the life science industry as at 2012. The firm development describes how the number of companies and employees has developed over the period, 1998-2012. Together, these aspects aim to give insights into the size, structure, development and performance of the Swedish life science industry between 1998 and 2012.

In addition, some insights into global trends are described based primarily on literature studies and public statistics. Such information is primarily added to the sections describing particular business segments (Chapter 5).

2 Methodology

2.1 Sectors

The characteristics of companies falling into the medical technology sector are that they develop medical products that are not drugs. The characteristics of companies falling into the pharmaceutical sector are that they develop drugs and various kinds of therapeutic products or methods. The biotechnology sector is characterised by companies developing the application of science and technology to living organisms as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services. The OECD definition of biotechnology activities has been used to identify biotech companies and the definition is listed at the end of the report. In the sector categorisation of each individual company, the approach or method used to solve a problem or satisfy a customer or patient need was often crucial to this categorisation. Together, these three sectors constitute what is known as the life science industry.



Due to the definitions of the three sectors, there are companies whose major activity can be categorised as belonging to more than one sector. For instance, there are many companies within drug discovery that could be defined neither as exclusively pharmaceutical nor as exclusively biotechnology companies. Therefore, each company has been classified into one specific business segment (narrower areas than the sectors which will described in the next section), whereas an individual company can be found in more than one sector. Thus it should be kept in mind that the business segments add up to the total number of employees, whereas the three different sectors do not.

A list of all companies included, and their categorisation by business segment appears in a separate attachment to the present report. The companies focusing on sales and marketing are in the attachment only divided into one of the three sectors. This results in an underestimation of biotechnology since all companies related to drugs are categorised as sales and marketing in the pharmaceutical sector even if they are marketing biopharmaceuticals.

The collection of data to build the company database was initiated in 1997 for the biotechnology and pharmaceutical sectors and in 2003 for the medical technology sector. Thus, the 1998-2003 result of the medical technology sector, as well as the data from the total life science industry over the period 1998-2003 should be interpreted with some caution since the firm population for 1998-2003 may be incomplete.

2.2 Business segments

The method used in this analysis means that each company has been individually categorised into only one of the business segments according to each company's main business. This leads to that companies with their main activity in business segments other than those listed below are not included in the study, even if they have such activities to some extent. As a result the study underestimates the number of employees in the industry and in the included business segments. This is a methodological compromise since it would be very difficult to accurately estimate the proportions of diversified companies falling within the delimitation of the business segments below.

Drug discovery, development, delivery and production

- Very few pharmaceutical companies discover and develop new drugs without using biotechnological tools. However, not all companies have the development of biopharmaceuticals, i.e. drugs based on large biological molecules such as proteins, as their goal. Rather, the large biological molecules are targets for the drugs developed. The drugs can be small molecules produced by organic chemical synthesis. The companies seek to develop new therapies to put on the market or license to pharmaceutical companies generating up-front and milestone payments, royalties and possibly revenues from sales on divided markets, depending on the agreement. Biomarkers to help identify patient populations that benefit from a specific therapy or do not have the same propensity for negative side effects are expected to become increasingly important. Included in this category are also substitute plasma and products for clinical nutrition.

- Companies in drug delivery are conducting research on how the active substances in medicines can be made to reach their target molecules in the body and how a satisfactory uptake of these substances can be ensured. Their clients are mainly companies involved in drug discovery and development. An increasing business area includes developing new formulations for existing drug substances, so that they can be better used for the same indications or for new ones. Using existing substances reduces development time, as they have already passed the regulatory process. The field of nanobiotechnology is expected to generate new solutions on how to administer drugs more specifically. The areas of polymer chemistry, nanotechnology and surface chemistry are examples that possibly will require more expertise in the future.

- Companies specialising in drug production which do not have their own research operations are also included. The use of biotechnology in the manufacturing of drugs is not included in this business segment. Instead, those companies are found in the biotech production business segment. Important issues include continuous development of cost-effective process and production technology as well as regulatory requirements.

In vitro diagnostics

- The companies develop tools and techniques for diagnostics and most of their customers are the healthcare sector, clinical laboratory analysis companies and end consumers for home use. The biotechnology diagnostic companies often develop antibody-based tests. Medical technology diagnostic products can be technical appliances for measuring or visualising diagnostic results (included in other business segments), or in vitro diagnostic tests which test a

sample of tissue or bodily fluids. A difference compared to companies developing new drugs is that the process from idea to commercialisation of diagnostic products, processes and services is usually much shorter.

Biotech medical technology

- Provides the healthcare sector with products within that part of medical technology which has a biotech basis according to the OECD definition, including equipment and instruments for in vitro fertilisation, blood management, cell therapy, plus the use of biodegradable biomaterials to replace or repair damaged tissue often referred to as tissue engineering and regenerative medicine.

CRO companies

- CRO (Contract Research Organisation) companies primarily include clinical research organisations dealing with products and services for assisting other companies in clinical trials and regulatory processes. The companies being assisted may be biotechnology, pharmaceutical or medical technology companies. Clinical research organisations need to be familiar with international regulations and regulatory bodies as well as having well-developed contacts in clinical research, hospitals and authorities. Some CROs have developed a technology platform or analysis system that is managed within the company and accessible to companies by contract research to help bring products through the regulatory system.

Biotech tools and supplies

- Develop products and services for use in production, research and development. This includes products and services relating to bioseparation, biosensors, biomolecular analyses and bioinformatics. Their customers mainly consist of other biotechnology companies, the pharmaceutical and medical technology sector and university research teams but also other industries basing their products on biological raw materials, for instance in the food, forestry and agricultural sectors. Their expertise lies within application of interdisciplinary expertise combining technologies such as electronics, ICT, optics and materials engineering with life science to develop their products and services.

Biotech production

The business segment can be divided into two sub-sectors as described below.

- Biotechnological production of biomolecules, cells or microorganisms for use in healthcare-related products such as diagnostics and pharmaceuticals. These are specialised manufacturing companies whose clients include the pharmaceutical sector, other biotech companies or research groups. The biomolecules are often enzymes or antibodies. The companies' core expertise is development of cost-effective production solutions - adapting their activity to internationally stipulated regulatory requirements on quality and safety, plus an ability to adapt to customer requirements.

- Biotechnology applied to industrial processes for large-scale biotechnological production, such as designing an organism to produce a useful chemical or using enzymes as industrial catalysts to produce valuable chemicals. Industrial biotechnology solutions tend to consume fewer

resources than traditional processes used to produce industrial goods. The chemical, forest, pulp and paper industry and the food industry has not been included since the core competence in those companies is not biotechnology, even if the technology is used to some extent. However, most of the development of biotechnological processes in these industries in Sweden does occur in large companies that do not have biotechnology as their core activity. There are few intermediary companies commercialising academic research in this field. Therefore, very few companies devoted to Industrial biotechnology are included in the present study but the intermediaries may prove important for the development of the field.

Agro-, environmental or food related biotechnology

The business segment can be divided into three sub-sectors as described below.

- Develop plant-related products utilising biotech methods, for example as tools in the cultivation work for plant or tree breeding. However, few companies use gene technology as a method for obtaining specific properties in the end products (genetic modification). Also included is plant protection based on naturally occurring microorganisms or biomolecules as well as the processing of land-based raw materials with the aid of biotechnology.

- Biotech solutions to environmental issues such as water purification, land decontamination (bioremediation) and waste management, as well as laboratory analysis. Customers to companies in this segment include municipalities, construction companies, and industries requiring such things as purification of water used in manufacturing processes. Companies within this field have very diverse focuses and it is therefore difficult to highlight a common core expertise. Some of these companies use non-pathogenic, naturally occurring micro-organisms to treat waste, water or soil and the laboratory analysis companies develop specific testing methods and analytical measurement tools, to measure toxic substances for instance. However, biosensors are included in the biotech tools and supplies business segment.

-The products of companies in the field of food related biotechnology include biotechnically-produced components or ingredients for the development of foods with positive health benefits, such as probiotics. Food products in this field are sometimes referred to as functional food. This denotes a product with a documented, well-defined, product specific diet-health relationship. The aim of these products is to reduce the risk of developing diseases rather than cure them. Examples of other possible areas found in the segment include use of enzymes in food processes or as additives, or the development of quality control in the food sector by means of new biotechnological techniques. These companies are often intermediaries between academic research and the food industry. They need both expertise within their niche, (within, say, microbiology, nutrition and process technology) and knowledge of potential markets, public attitudes/demand and the needs of the food industry. The food industry, which uses biotech tools in its production processes for example, is not included in the population.

Healthcare facility products and adaptations as well as single-use devices

The business segment can be divided into four sub-sectors as described below.

- Companies producing machines, fittings and furniture for health services such as machines for disinfection and sterilisation, lighting, patient lifts (transfer aids), hygiene systems, examination

couches and treatment tables. To be included, their major business must be products specifically for the healthcare sector. The companies are often manufacturing companies with an understanding of needs within the healthcare sector.

- Companies dedicated to surgery or medical appliances within the field of ophthalmology are also included in this business segment. The required expertise may include ophthalmic surgical technology like cataract surgery. Products include laser vision products, eye surgery products and computer software for imaging the inside of the eye. The latter may be used for diagnosing eye conditions.

- Companies developing instruments and technical appliances used by dentists as well as disposables and supplies for use in dental clinics. Dental implants are found in the business segment “Implantable devices”. On the other hand, dental laboratories and such things as toothbrushes and toothpaste are not included.

- Disposable products used in patient care, such as dosage cups, catheters, hypodermic needles, sponges, contrast agents, incontinence and wound care products, syringes, gloves etc. are included as are reusable products such as surgical instruments. These companies are often manufacturing companies. Knowledge of industrial processes, sterilisation techniques and materials science is important. Characteristic of some companies is knowledge of the processes behind wound healing and the optimal conditions for wound care.

Implantable devices - active and non-active

- Implantable dental, orthopaedic or other medical devices are included in this segment. They may be biologically active, like pacemakers and bone-anchored hearing aids, or non-active, like hip and knee joint replacement and cardiac stents. Specialist expertise is needed in various medical fields, materials science and tissue response to materials (risk of infection). Materials may include titanium, ceramics and steel. Implants are usually developed in close collaboration with the healthcare sector.

Anaesthetic and respiratory devices

- Development of anaesthetic equipment and solutions for supervision or control of respiration. The products are mainly used for critically ill patients, i.e. intensive care (respiratory equipment) and in operating theatres (anaesthetic and/or respiratory equipment). Anaesthetics may be delivered to the patient intravenously or by inhalation. Products are developed in a combination of medical expertise, including anaesthetic properties of different gases, as well as expertise in a number of engineering fields such as mechanics and electronics for pneumatic systems, valves and sensor technology and computer programming for monitoring and control systems.

Electromechanical medical devices

- Technical equipment used for diagnostics, patient care and supervision or visualising of conditions. This business segment includes a broad range of products used in many medical fields such as critical care systems, perinatal monitoring and dialysis equipment. Many companies are large with diversified business and may also develop products falling into other business segments. The companies identified require technical as well as medical expertise.

Radiation devices - diagnostic and therapeutic

- Develop products used in nuclear medicine such as devices for radiotherapy and radiology examinations, such as magnetic resonance imaging, computed tomography, positron emission tomography, X-ray and ultrasound devices. Laser therapy devices are also included in this business segment. The companies identified require technical as well as medical expertise.

Information and communication tools

A way to describe the different types of ICT solutions being developed for use in the health service is dividing the products and services into: 1) Administrative systems, 2) Electronic health records, 3) Technical ICT as well as 4) Personal health related products for end consumers.

- Administrative systems includes tools for documenting and organising the healthcare process, communication between patients and the health service regarding such things as scheduling appointments, monitoring adherence to the prescribed drug intake and exchange of information regarding specific conditions.

- Electronic health records facilitate the handling and integrating of large volumes of information concerning patients such as medical history, medication, allergies, laboratory test results, radiology images, vital signs, personal statistics like age and weight. It may also include analytical tools for clinicians that for example can function as diagnostic support or monitoring of patients health status, link to research tools, quality registers, clinical studies and trials etc., sometimes referred to as medical informatics.

- Technical ICT improves the performance or use of medical devices for instance by developing algorithms for better image analyses or software for deciding on radiation dosages and the integration of data from medical devices to electronic health records. Here are also tools for medical training purposes for personnel in the healthcare sector such as for instance virtual surgery systems found. ICT home care solutions are also included in this category.

- Personal health related products for end consumers include for instance personal health diaries/records, tools to monitor sleep, pulse etc. as well as for preventive care including food and exercise monitoring. Here are also ICT solutions for therapeutic purposes included such tools as those for cognitive training.

Extensive knowledge about medicine, medical devices and their use in the health service and about healthcare provision is vital to the development of most of the above described tools. Many of especially the administrative ICT solutions are developed by large diversified ICT companies which also develop products for many other businesses. Those companies are thus not included in this analysis unless the health care sector and life science applications are the primary focus of the company.

Assistive products for disabled people

- Develop products such as walking aids, wheelchairs, prosthesis, hearing aids which are not bone-anchored and orthopaedic devices. Providers of fittings and service concerning orthopaedic devices connected to the healthcare sector are not included.

2.3 Activity category

The companies have been also categorized into five different activity categories:

1 Exploratory research and development
2 Incremental product development
3 Consultancy
4 Manufacturing
5 Sales and marketing

2.4 Number of employees

What is shown as "number of employees" in the report is the mean value of the number of full-time equivalent (FTE) employees each year included, i.e. the number reported by companies in their annual report to the Swedish Companies Registration Office. The actual number of people employed in companies may be 20-30 percent higher due to part-time posts, leave of absence etc.

The size of companies or operation, measured by number of employees, is given as a bubble where the size of the company or operation is proportional to the volume of the bubble.

2.5 Visualisations

Bubble diagram

The bubble diagram used in this study (Figure 6) shows four variables simultaneously:

- Activity category (vertical axis)
- Business segment (colour)
- Company size in terms of the number of employees (bubble size, volume proportional to the number of employees)
- Exports: No exports, Some exports, and Significant exports

In the statistics used, the export data [million SEK per year] for each company is given in the following intervals: 0.001 – 0.249; 0.250 – 0.999; 1 – 1.0; 2 – 4.9; 5 – 9.9; 10 – 49.9; 50 – 99.9 as well as more than 100.

The mean value of the interval for the export data given in absolute numbers have been divided by the net turnover for each company giving the export in relation to turnover [%]. For the graphical illustrations in this report three different export categories have been used: 'No exports', 'Some exports', and 'Significant exports'. Where "Some exports" is defined as exports of 1-50 percent of annual net turnover and "Significant exports" as more than 50 percent in relation to company net turnover. All companies with exports of more than SEK 100m per year have been placed in the "Significant exports" category, even if their turnover is more than SEK 200m per year.

Companies with fewer than 500 employees and several activity categories within the company have been placed in the activity category which is highest on the vertical axis. This means if the

company has both incremental product development and manufacturing activities, they appear under “Incremental product development” on the vertical axis. Following contact with the companies, those with more than 500 employees have been divided into different activity categories in the bubble diagram. They are thus separate bubbles, showing such things as the number of employees within manufacturing. The bubble highest on the vertical axis is downsized according to the number of employees in other activity categories and new bubbles are created for those units.

Readers may thus draw their own conclusions based on different combinations of the variables.

Dynamic diagrams

The database for the biotechnology and the pharmaceutical industry dates back to 1997 including no longer existing companies as well as number of employees and financial data for the companies. The medical technology database was largely constructed in 2003. Thus, data for 1998-2003 is based on the 2003 company population. Thus keep in mind, that a limited number of old medical technology companies may be missing in the dataset for 1998-2003, under-estimating the size of the medical technology sector for those years. The number of companies is calculated for each year depending on the criteria selected for analysis, such as size class and business segment and includes the company population each year, i.e. also including companies that today have ceased their activities in Sweden.

Map

In the map visualisation (Figure 5), all bubbles in the diagram are distributed by municipality according to their geographic location. Companies may thus occur with several bubbles in the map according to the size (number of employees) and geographic location of each company’s’ different company facilities. They have been randomly distributed within each municipality. Companies with operations in different municipalities are thus shown as bubbles on the Swedish map, where the volume is proportional to the number of employees in each municipality.

2.6 Assessment

The scope of the analysis and also the identification of potential companies to include have been ironed out in discussions and collaboration with organisations such as: Västra Götalands-regionen, GöteborgBIO and Business Region Göteborg; Region Skåne and Invest in Skane; Stockholm Uppsala Life Science, Stockholm Business Region, Stockholm Life and Uppsala BIO; Biotech Umeå as well as BioMedley and New Tools for Health.

The Swedish trade associations SwedenBIO, Swedish Medtech and Läkemedelsindustri-föreningen LIF, have contributed with both company listings and other important insights to the industry through interviews. Also, the Pipeline report[1] performed by SwedenBIO with support from VINNOVA and Business Sweden has been an important source of information about the pharmaceutical industry in Sweden. An in depth analysis of trends regarding e.g. indication

[1] www.swedenbio.com

areas and other trends in the industry has been performed in collaboration with Business Sweden.

Companies which have their major activity within the previously described selection of business segments with at least one employee in 2012 are included in the bubble diagram and listed in an attachment to the present report. Similarly included in the dynamic diagrams are companies with employees in any of the years 1998-2012 and whose major activity is in the previously described selection of business segments.

Companies devoted to sales and marketing of life science products are not included in the visualization but are included in much of the analyses in the report and listed in the attachment.

Subcontractors to companies within the selection of business segments which do not have their core activity within these fields of expertise are not included. This may apply to such enterprises as design companies, companies within manufacturing (if the operation is not entirely concentrated on included business segments), ICT, mechanical, optics and electronics companies, PR agencies, venture capital companies and patent and business advisers. In recent years, a number of staffing companies providing personnel to the life science industry have also appeared. The scope of all these activities is difficult to estimate as many of these companies are broad serving many other businesses and they have thus not been included in the company population. Also excluded are companies in the chemical, pulp and paper and food industry which may have some biotech activities, but not as their core competence.

Laboratory equipment not specifically designed for use in the biotechnology, pharmaceuticals or medical technology sectors is not included in the bubble diagram. This for example includes companies developing pH meters, magnetic stirrers, mass spectrometers or even those designing and building whole laboratories.

Companies conducting laboratory analysis services, often service laboratories to the healthcare sector, plus orthopaedic and dental laboratories and companies developing products sold by opticians have not been included at all in the present study. Companies developing laboratory equipment which can be used in many sectors are also not included in the analysis.

There are also many companies with no employees still active according to Swedish Companies Registration Office; these are not included in the bubble diagram or figures mentioned above.

Details of business segments, activity categories and markets are not available in general statistics. These require assessment based on information from different sources, for instance publicly available information on the companies' webpages. Also, about one third of the companies have been contacted individually in order to assess business segments and activity category. The categorisation was made by the author.

3 The Swedish Life Science industry – overall picture and dynamics

3.1 Structure, size, dynamics, supply of competence and financing

Both in countries with a long tradition of innovation in the life science area and in other countries with a rapidly increasing life science knowledge base, substantial efforts are made and public investments increased to spur knowledge creation, innovation and industrial development[2]. The life science industry is an important contributor to Swedish exports, knowledge intensive employment and generates high value added products.

Number of companies and employees

In 2012, the industry encompassed 40 764 employees in 1 487 companies with a core competence in life sciences. Indirectly many other companies are closely linked to the industry providing products and services as suppliers and consultants used by the life science companies. Partners and customers of the life science companies are also often actively involved in the innovation processes, in Sweden and abroad. In the present analysis however, only the companies with a core competence in life sciences, and the majority of their business in life sciences are included. Also, only their activities in Sweden are included. The total number of companies identified in the present study as active in research and development, product development, consulting or manufacturing within the included business segments of biotechnology, pharmaceuticals and medical technology in Sweden is 791, with a total of 29 652 employees. Companies dedicated to sales and marketing, often also managing clinical trials in the region, employ 11 113 personnel in 696 companies. In Figure 1 below, the overall development of the size of the life science industry 1998-2012 is shown to the left. To the right the development of the number of employees in different size classes is seen for the life science industry excluding sales and marketing companies.

If we compare the number of employees to the result from similar analyses of other industries[3] we see that there are slightly less employees in the mining and minerals industry and slightly more employed in the chemical, maritime and metals industries than in the life science industry. The energy and clean tech industries are more than twice as big, automotive three times larger and the ICT-industry have more than 130 000 employees.

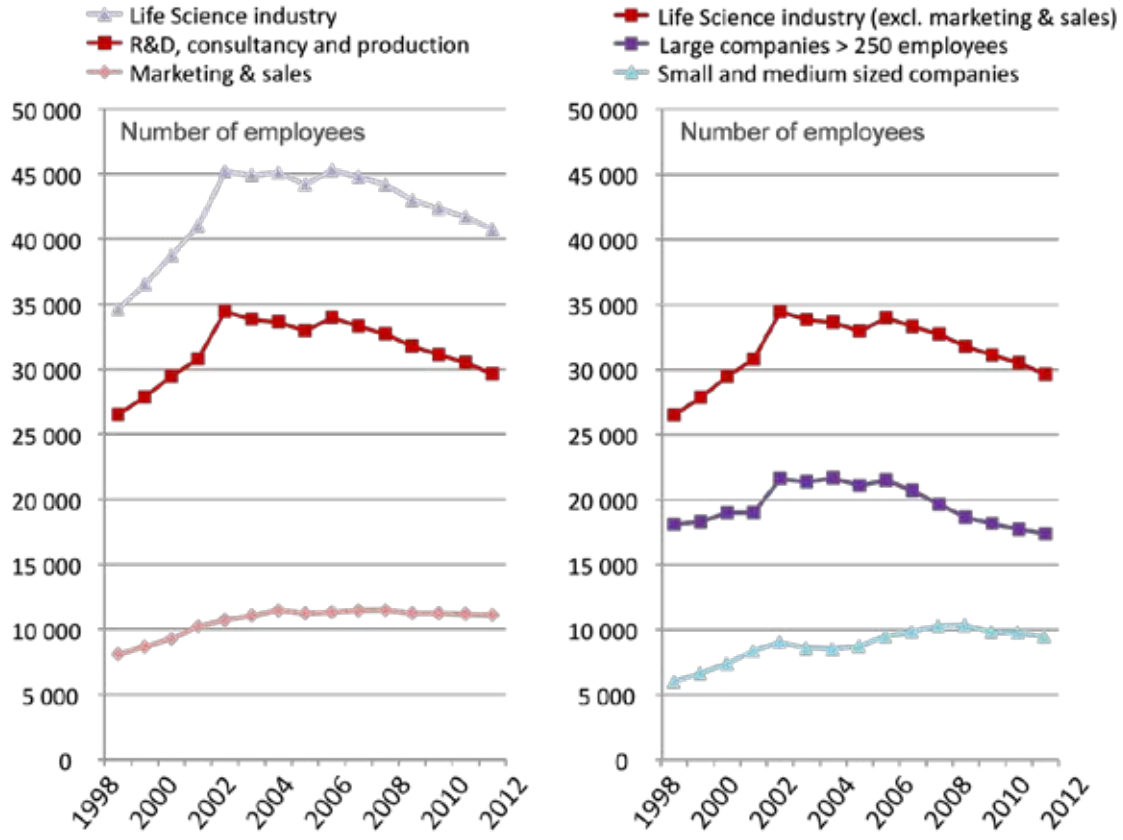
[2] www.vinnova.se\life_science_benchmarking
[3] http://www.vinnova.se/sv/Om-VINNOVA/VINNOVA-och-omvarlden/Trender-i-Sveriges-kunskapsintensiva-naringsliv/

Table 1 Number of companies and employees for a selection of branches of industry analysed in a similar way as in the present analysis (only Swedish operations are included) *

INDUSTRY BRANCH	NUMBER OF EMPLOYEES	NUMBER OF COMPANIES
MINING AND MINERALS	22 500	440
LIFE SCIENCE	29 700	791
METALS	33 000	180
MARITIME	34 000	2150
CHEMICALS	34 000	450
ENERGY	71 000	1121
CLEAN TECH	74 700	1553
AUTOMOTIVE	93 000	451
ICT	132 100	2704

** Automotive include companies > 19 employees, ICT include companies > 4 employees, the others include all companies with employees*

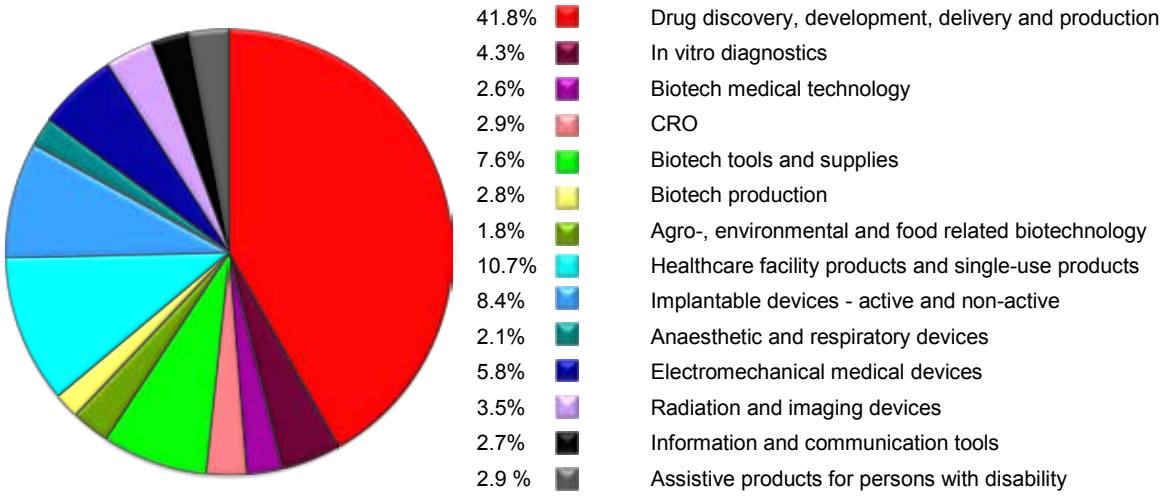
Figure 1 Number of employees in the total life science industry and in the part of the life science industry involved in R&D, consultancy and production (i.e. excluding sales and marketing) years 1998-2012



The life science industry had the most employees in 2006, 45 300, and since then the number of employees has declined by 10 percent. If we look at companies involved in R&D, consultancy or production, i.e. excluding sales and marketing companies, the size of the industry peaked in 2002 with about 34 900 employees, i.e. the number of employees has since then decreased by 15 percent or more than 5 200 employees. More than 90 percent of that decrease is due to the

downsizing of AstraZeneca by almost 4 800 employees. As is seen in Figure 1 the development of the number of employees in the small and medium sized companies have increased until 2007 and then levelled off, in total an increase of almost 60 percent or about 3 550 employees.

Figure 2 Proportion of employees of the business segments in the life science industry in 2012 (excluding sales and marketing)



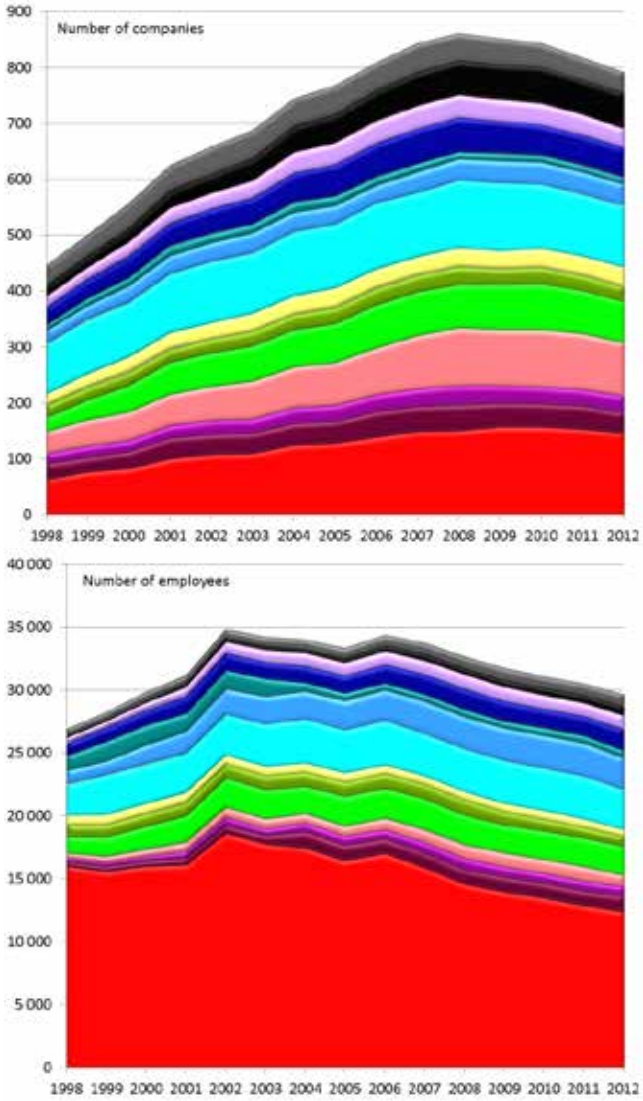
Again excluding sales and marketing companies, the drugs business segment dominates the life science industry with 42 percent of the employment, followed by healthcare facility products (11 percent), implantable devices (8 percent) and biotech tools (8 percent).

In Figure 3 below, the development of the number of companies and employees linked to particular business segments is illustrated. This will be analysed in some detail in coming chapters, especially in Chapter 5. The drug discovery development, delivery and production segment (hereafter called the drugs business segment) has however decreased its number of employees the most, primarily due to the changes in AstraZeneca. The industry, excluding sales and marketing, has in total declined by about 4200 employees the latest five-year period; the downsizing of AstraZeneca is responsible for 76 percent of that decline and for more than 90 percent of the decline in the drugs business segment. There is however a number of business segments counteracting the negative development of AstraZeneca.

The growth in number of employees over the entire time period studied (1998-2012) is largest for biotech tools and supplies and implantable devices, an increase by 1900 and 1400 employees respectively. Segments with a reduction in number of employees are anaesthetic and respiratory devices and, to a lesser extent agro-, environmental and food related biotechnology and biotech production.

The number of companies has grown for all business segments but assistive products for persons with disability staying constant at 37 companies. The most significant increase is for the drugs segment followed by CROs and ICT tools.

Figure 3 Number of companies (top) and employees (bottom) in the business segments of the life science industry years 1998-2012 (excluding sales and marketing)



The structure of the life science industry

The bubble diagram shows all companies active in exploratory research and development, incremental product development, consulting or manufacturing within the included business segments of biotechnology, pharmaceuticals and medical technology in Sweden in 2012. The bubble size is proportional to the number of employees and the colours shows what business segment the company belongs to. Companies with more than 500 employees are divided into

different bubbles based on the size of activities according to the activity categories on the vertical axis.

The structure shows that it is mostly small- and micro-sized companies and consultancies that have no export whereas all of the large companies have some or significant exports. Companies involved in exploratory R&D are found in all business segments. There is a slight tendency for companies in incremental product development to more often be found in business segments in the medical technology sector. The presence of a number of contract manufacturing companies in the pharmaceutical field together with some of the large companies manufacturing sites contribute to the many red manufacturing bubbles seen in the bubble diagram. Compared to many other branches of industry[4], the life science industry has an extremely large proportion of the industry involved in exploratory R&D. Almost 50 percent of the companies are research-intensive and have activities in exploratory R&D.

The public R&D investments in medicine, pharmacology, odontology, veterinary medicine and biotechnology[5] at Swedish universities in 2011 was SEK 9.4bn which corresponds to more than 30 percent of the total public spending on R&D (SEK 29.7bn). The corresponding proportion for engineering sciences[6] was 23 percent.

Information about the R&D investments of the whole life science industry is unfortunately not available, but the figure for the pharmaceutical industry is SEK 7.8bn, or almost 10 percent of the total investment in R&D by companies in Sweden (SEK 81.1bn). This can be compared with for instance computers, electronics and optics with 19 percent and automotive with 23 percent. When it comes to the number of PhDs employed in the industry however, the proportion for the pharmaceutical industry is as high as 18 percent, automotive 12 and computers, electronics and optics 2 percent.

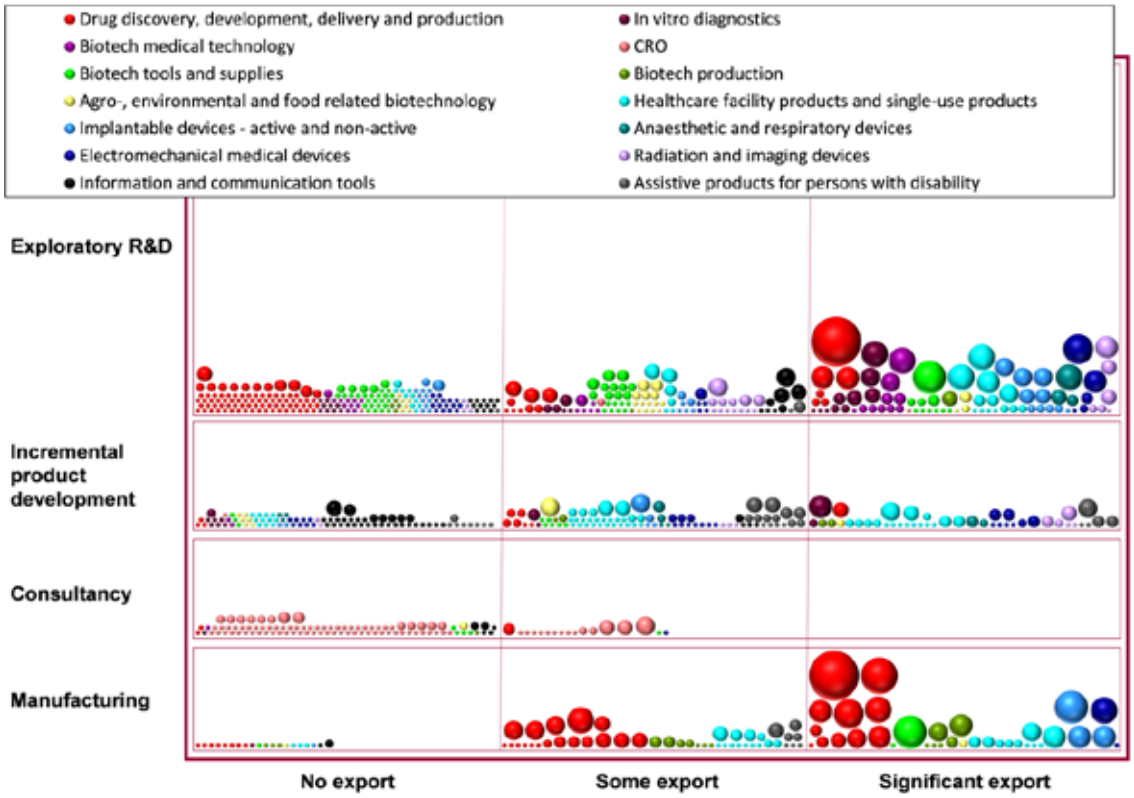
When it comes to Swedish life science industry export, it is only possible to identify pharmaceuticals and medical technology in the public records (Statistics Sweden), not biotechnology products. Together the two sectors contribute 7.7 percent of the Swedish export in 2012, 2.8 and 4.9 percent for medical technology and pharmaceuticals respectively. This can be compared with 5.2 percent for telecom, radio, TV-appliances etc., 10.8 percent for automotive and 8.0 percent for pulp and paper.

[4] http://www.vinnova.se/sv/Om-VINNOVA/VINNOVA-och-omvarlden/Trender-i-Sveriges-kunskapsintensiva-naringsliv/

[5] Medicine, surgery, morphology, physiology and pharmacology, social medicine, microbiology, biotechnology, other medicine, odontology, pharmacy, veterinary medicine, healthcare services in society

[6] ICT, technological physics, electrotechnology, electronics and photonics, chemical engineering, biotechnology, mechanics, material science, architecture and the built environment, industrial economics, other engineering

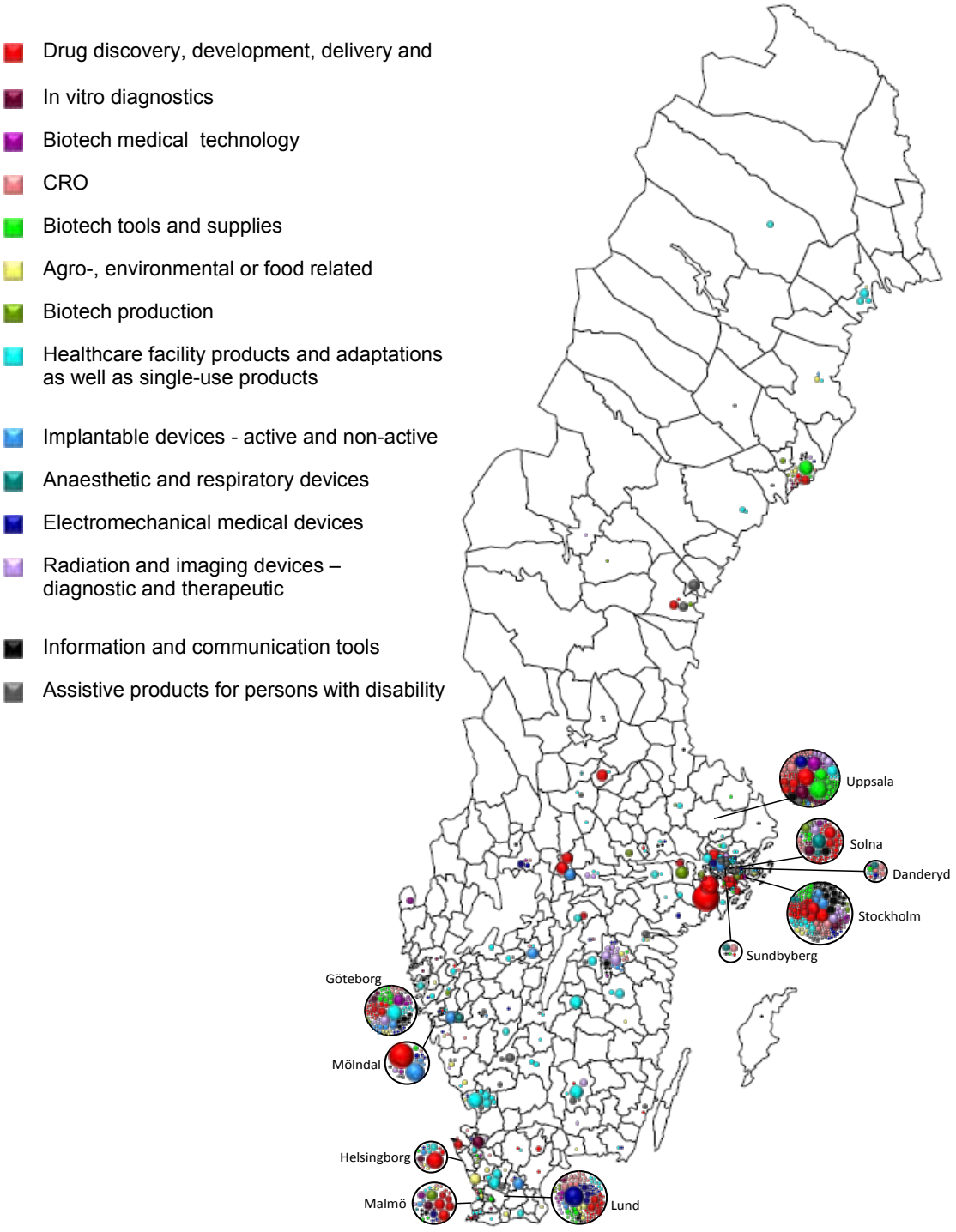
Figure 4 Bubble diagram showing all companies active in exploratory research and development, incremental product development, consulting or manufacturing in the included business segments of the life science industry in Sweden in 2012, companies with exports representing more than 50 percent of the net turnover or more than SEK 100m are categorised as having significant export [the bubble size (volume) is proportional to the number of employees for each company facility and the colour represents the business segment]



The geography of the life science industry

In the map below the geographic distribution of the life science companies (excluding sales and marketing) is shown. Each company establishment is distributed to the municipalities where they are located and with a bubble size proportional to the number of employees. The companies are clustered to the regions surrounding Stockholm, Gothenburg, Malmö/Lund, Uppsala, Strängnäs/Södertälje, Umeå and Linköping. Manufacturing units are more geographically dispersed.

Figure 5 Geographic distribution of companies active in exploratory research and development, incremental product development, consulting or manufacturing within the included business segments of the life science industry in Sweden in 2012 [the bubble size (volume) is proportional to the number of employees for each company facility and the colour represents the business segment]



For some regions the pattern with agglomerations of some of the business segments indicates some degree of regional specialisation. This will be discussed further in Chapter 9.

Participation in the EU Seventh Framework Programme

The life science companies, compared to other Swedish industries, very frequently participate in the EU seventh framework programme (FP7). Of in total ten studied industries[7] no one comes near the 79 companies with in total 154 participations in life sciences[8]. Clean tech comes closest with 62 companies with 114 participations. This is perhaps to be expected considering the research intensity of the industry, the number of academic spin-offs with researchers employed as well as the size and focus of FP7 on health and life science research. In Appendix all life science companies participating are listed. As expected, Health is the largest research theme with 76 participations, then follows projects in People (31 participations, e.g. Marie Curie Actions), NMP (Nanosciences, nanotechnologies, materials and new production technologies, 18 participations), ICT (Information and Communication Technologies, 11 participations) and SME (Research for the benefit of SMEs, 10 participations). Most participating companies are found in the Stockholm/Uppsala region as well as Lund and Gothenburg.

As is seen in the bubble diagram below, companies participating in FP7 are predominately small companies belonging to the business segments drug discovery and biotech tools. Large companies include AstraZeneca (14 participations), Swedish Orphan Biovitrum (1), Elekta (1) and GE Healthcare Bio-Sciences (1). Medical technology companies participating for example include Bactiguard, Permobil, Gems Pet Systems, St Jude Medical, Raysearch Laboratories and Hotswap. Six small companies are coordinators of FP7 projects: Olink, Saromics Biostructures, Viscogel, Newron Sweden (previously Neuronova), Vironova and Bohus Biotech.

Geographically the companies participating are primarily found in the Stockholm and Uppsala regions, but also with companies in Gothenburg and Lund participating. In relation to company population, Uppsala has the largest proportion participating.

Innovative Medicines Initiative (IMI) is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients. IMI is a partnership between EFPIA and EU. The projects involve extensive collaborative efforts between academia and industry. The initiative has a total budget of EUR 2000m (half from EU). Players such as academia, patient organisations and industry can suggest research areas which are reviewed by a scientific committee, primarily including academic scientists. The committee advices the governing board of IMI - the main decision-making body with equal number of representatives from EFPIA and the European Commission - which then decides which areas will be included in a call procedure. Partnerships between academia, industry, healthcare and regulatory bodies sends in tenders and the governing board then decides on which initiatives will receive funding. Typically projects run for five years and covers EUR 7-40m, has 20-30 partners and typically involves several Big Pharma companies per project. Swedish participants are in fifth place in Europe after UK, Germany, France and the Netherlands in terms of the funding received from IMI. Of 97 applications with Swedish applicants, 52 have been granted a total funding of about EUR 84m (SEK 738m), i.e. a success rate of 54 %. The granted applications are primarily

[7] http://www.vinnova.se/sv/Om-VINNOVA/VINNOVA-och-omvarlden/Trender-i-Sveriges-kunskapsintensiva-naringsliv/

[8] Industrial research institutes have in the present study been excluded from the FP7 analysis

focused on diabetes, antibiotics, cancer and inflammation. AstraZeneca is a frequent partner in IMI projects with participation in 29 of the on-going 40 projects.

Figure 6 Bubble diagram for companies in the life science industry (excluding sales and marketing) participating in the EU Seventh Framework Programme (top) compared to the entire industry (bottom)

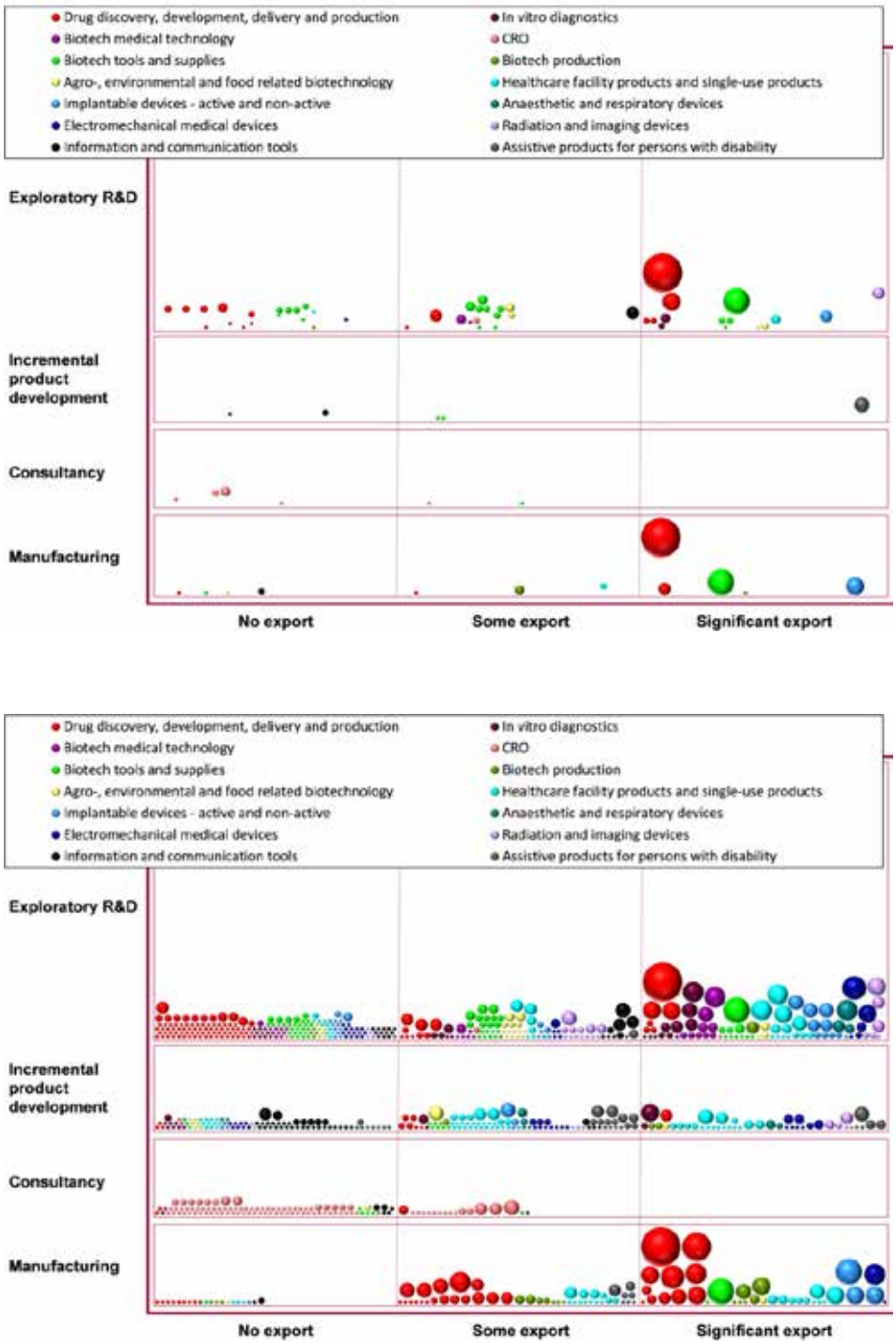
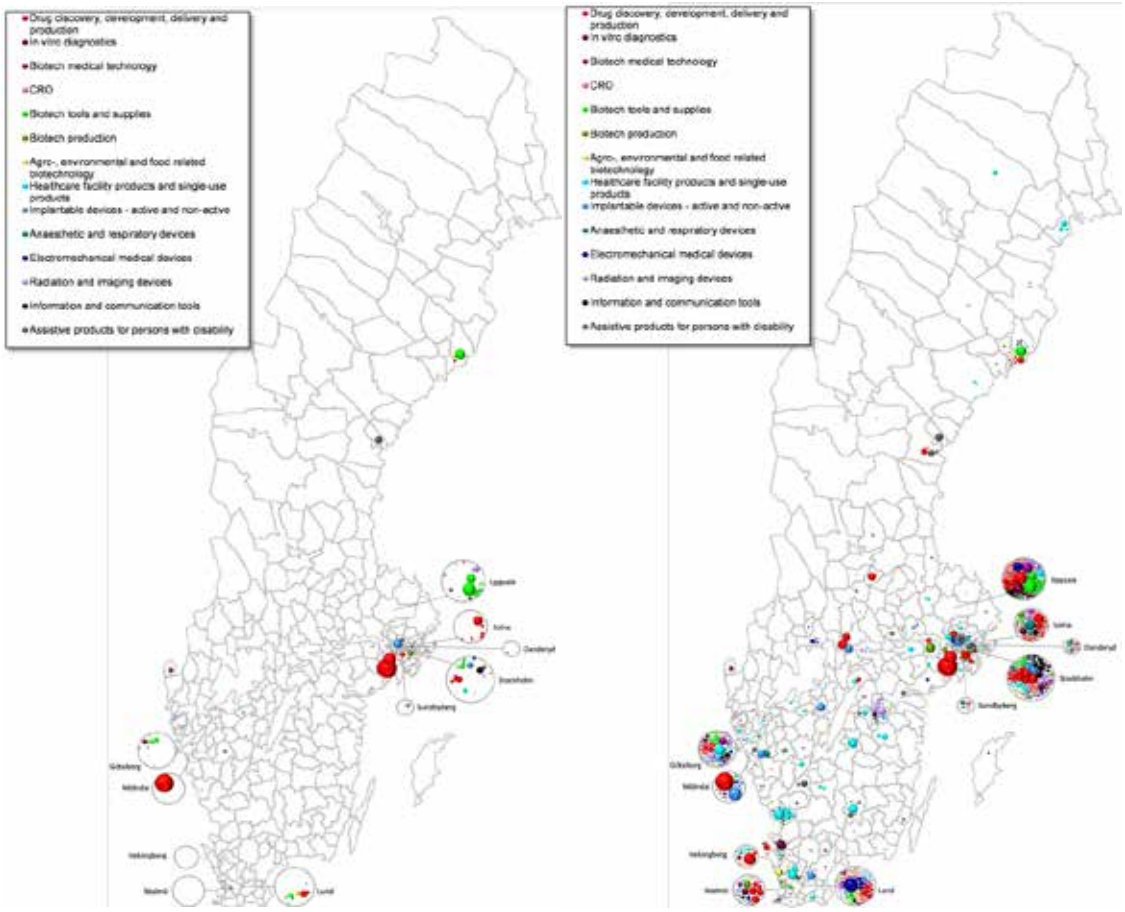


Figure 7 Geographic distribution of companies in the life science industry (excluding sales and marketing) participating in the EU Seventh Framework (left) compared to the total industry (right)



Competence supply

The employment in the Swedish life science industry is changing in absolute numbers but also regarding an increased proportion of the employment being in SMEs and among the larger companies more companies are foreign-owned. The employment structure has also changed regarding educational level. The changes in the structure of the life science industry are likely to also change the recruitment pattern. For the educational system it is thus interesting to monitor the trends in the industry. At AstraZeneca in Gothenburg, as many as 300 employees are of other nationality than Swedish and coming from 30 different countries.

In a previous VINNOVA study[9], the educational level of the employees in the life science companies identified 2009 was mapped. Of the about 31 500 employees in 700 companies with activities in R&D, consultancy or manufacturing identified in that study, 3 200 were PhDs, i.e. nine percent of the employees in that part of the life science industry. Of the PhDs, 2 600 were employed in pharmaceutical or biotech companies and 600 in medical technology. Apart from the PhDs, almost 16 800 employees had a post secondary school education. Comparing the

[9] http://www.vinnova.se/sv/Aktuellt--publicerat/Publikationer/Produkter/Life-Science-companies-in-Sweden/

years 2000, 2003, 2006 and 2010 the result showed increasing proportions of the employees with higher educational level, i.e. above secondary school and reclining proportions with a lower educational level. This pattern is the same for both pharmaceuticals/biotechnology and medical technology. The number of employees with higher educational level has increased by 25 percent 2000-2010 corresponding to about half of the employees in 2010. The number of PhDs has grown by about 1 000 which correspond to a 49 percent increase.

During the same time period the number of persons with a graduate education in subjects relevant to the Life Science industry, the health service and academic research in life sciences increased by more than 70 percent. In 2010 the number of PhDs graduating was about the same size as the total increase in the analysed life science companies, i.e. about 1000 graduated in one single year.

The trend with an increasing proportion of the employees in the life science industry with a graduate education is seen in all three major Swedish life science regions. This applies to both the combination of biotechnology & pharmaceuticals and medical technology.

Venture capital firms and business angels

The number of Swedish based VC-firms active on the Swedish life science market is fewer than a few years back. The ones still investing in young innovative companies include for instance Industrifonden and HealthCap. There is also a trend of investments in later development phases leading to fewer and larger investments.

Other investors include business angels with their own funds such as Bengt Ågerup (previously Q-Med) with the investment company Nxt2b AB and Bo Håkansson with Farstorp Invest AB. Several foreign VC companies are active on the Swedish market, for instance a number of Danish VC companies as well as firms from other countries, such as Phase4 Ventures (UK), TPG Biotech (US), TVM Capital, Bridgepoint Capital, 3i Nordic and Scottish Widows Investment Partnership (UK). Also, the Swedish VC companies are raising their funds internationally. Below a number of VC-firms and their life science portfolio companies are listed. Other players investing in early phase projects are Almi, the holding companies of the universities and other organisations and companies closely linked to the universities, not listed in Table 2 below. An example is Karolinska Development AB with a deal-flow agreement with for instance Karolinska Innovations AB and a portfolio consisting of 35 projects, of which 16 pharmaceutical projects are in clinical development with 11 projects in Phase II.

Table 2 Examples of venture capital firms active on Sweden market and their life science portfolio companies 2014

VENTURE CAPITAL FIRM	SWEDISH PORTFOLIO COMPANIES
HEALTHCAP	Aerocrine, Affibody, Bonesupport, Cardoz, Cebix, LTB4 Sweden, MIPS, Orexo, OxThera, Trimb Healthcare and Wilson Therapeutics
INDUSTRIFONDEN	Airsonett, Amra, Bactiguard, Avidicare, Bonesupport, Boule Diagnostics, CellaVision, InDex Pharmaceuticals, Medtentia, Oncopeptides, OxThera, Pharmalink,RxEye, ScandiDos, TrialBee
SLS INVEST	Gyros, Medical Vision R&D
INVESTOR GROWTH CAPITAL	Aerocrine, Affibody, Atlas Antibodies, Biotage, Neoventa Medical, Scibase
SEB VENTURE CAPITAL	Airsonett, Avidcare, Index Pharmaceuticals, Neoventa Medical, Scibase, TSS
INNOVATIONSKAPITLAL	Alligator Bioscience, Bonesupport, Cellectricon, PBM

Source: Websites of Venture Capital firms

3.2 AstraZeneca

AstraZeneca is the seventh largest pharmaceutical company in the world with sales in 2012 of about USD 28bn: 38 percent in the US, 23 percent in Western Europe, 21 percent in emerging markets and 18 percent in the rest of the world. AstraZeneca today employs around 50 000 people worldwide: 13 percent in the UK, 31 percent in continental Europe (12 percent are employed in Sweden), 29 percent in the Americas and 27 percent in Asia, Africa and Australasia. The R&D investment is about USD 4bn each year. In the beginning of 2012, the number of employees involved in R&D was, according to AstraZeneca, 12 400. The same year the number of employees in Sweden was 6 232 of which about 3 000 worked in the manufacturing unit in Södertälje. More about Big Pharma and AstraZeneca is found in Sections 5.1 and 8.1.

Reduced dominance of AstraZeneca and Pfizer in the Swedish life science industry

Table 3 The AstraZeneca proportion of the pharmaceutical and life science industry in Sweden 2008 and 2012

	NUMBER OF EMPLOYEES 2008	ASTRAZENECA PROPORTION [%] 2008	NUMBER OF EMPLOYEES 2012	ASTRAZENECA PROPORTION [%] 2012
ASTRAZENECA **	8 419		6 232	
TOTAL LIFE SCIENCE INDUSTRY	44 195	19	40 764	15
LIFE SCIENCE INDUSTRY (EXCLUDING SALES & MARKETING)	32 717	26	29 652	21
PHARMACEUTICAL INDUSTRY	21 728	39	17 287	36
PHARMACEUTICAL INDUSTRY (EXCLUDING SALES & MARKETING)	16 681	50	13 918	45

** Life science industry: pharmaceuticals, biotechnology and medical technology*
*** The closing of the R&D operations in Södertälje have not yet come into full effect in the 2012 data*

The Big Pharma companies AstraZeneca (in Sweden with an origin in Astra) and Pfizer (in Sweden with an origin in Pharmacia) have become less and less dominant in the Swedish life science industry in terms of employment. AstraZeneca employed about 30 percent of the life

science employees all years 1998-2005 (excluding sales and marketing) and the corresponding proportion for Pharmacia went from 21 percent of the industry in 1998 to 9 percent in 2005 as part of Pfizer. In 2012 Pfizer employed 2 percent of personnel in the life science industry excluding sales and marketing and AstraZeneca 21 percent[10]. In relation to the total Swedish life science industry, the corresponding drop in Swedish employment for the two corporations is shown in the Table below.

Table 4 The proportion of employees for AstraZeneca and Pfizer/Pharmacia of the total life science industry in Sweden 1998, 2005 and 2012 [percent]

	1998	2005	2012
PFIZER/PHARMACIA	16.4	6.4	1.3
ASTRAZENECA	23.0	22.4	15.3
TOGETHER	39.4	28.7	16.6

The innovation processes in Big Pharma companies with several R&D-sites includes collaboration between different nodes in the company and external players. Lund was the primary node for the development of products such as Symbicort, Oxis, Pulmicort and Rhinocort addressing respiratory conditions. Gothenburg was amongst others the primary node for R&D leading to the heart medicine Seloken as well as Losec and Nexium for treatment of reflux disease and peptic ulcer. Astra Zeneca has had difficulties in refilling its pipeline to the extent that will compensate for the sales decline due to major products like Nexium and Seroquel losing their patent protection. Previous setbacks have included Iressa (cancer, now however used effectively for a smaller patient population than intended using companion diagnostics), Exanta (thrombosis, which after approval turn out to cause some patients liver damage), Galida (diabetes, had completed several phase III clinical trials when it was discontinued) and NXY 059 (stroke, second phase III trial indicated no significant activity).

The AstraZeneca pipeline includes 99 projects[11], of which 85 are in the clinical phase of development and 14 are either approved, launched or filed. During 2013, 33 projects progressed to their next phase and 15 projects were withdrawn. In 2013 AstraZeneca reported that 11 new molecular entities have entered Phase III trials or registration. AstraZeneca in the future aims to source at least 40% of their pipeline from outside own laboratories, i.e. biotechnology firms, research institutions and other pharmaceutical companies.

At the previous AstraZeneca site in Lund, now reside other life science players. Together they employ about as many as AstraZeneca did when it was announced that the unit was going to be closed. Under the name Medicon Village part of Lund University (cancer research), parts of the regional authority, Region Skåne (regional cancer centre and biobanking centre), Lund Life Science Incubator, the head office for European spallation source (ESS), and a number of life science companies have moved established operations to the premises. A few companies started by AstraZeneca alumni are also located there.

[10] The closing of the R&D operations in Södertälje have not yet come into full effect in the 2012 data
[11] AstraZeneca annual report 2013

The closing of the units in Lund and Södertälje will, and already has, lead to a reduction of the life science industry in Sweden. Even if part of the life science industry is expanding those positive trends cannot at present counteract the large decline in AstraZeneca. About one third of the employees in Södertälje losing their jobs had a graduate education with niched competencies. Apart from the directly employed losing their jobs the reduction of life science activities in the region will also affect consultancies, staffing companies and other suppliers of products and services, leading to secondary effects on the life science labour market.

Figure 8 Available information regarding the previous employees at the Lund site (892 employees) at the time of closing the site (situation December 2011) and the AstraZeneca R&D personnel (1213 employees) becoming redundant during 2012 (situation August 2013) [N/A means that no information is available]

Lund 892 employees (Dec 2011)

Södertälje 1213 employees (Aug 2012)

Source: AstraZeneca (2011) [12] *and Trygghetsrådet via AstraZeneca (2012)*

Figure 8 summarises the information available regarding the personnel previously employed in Lund as well as those in AstraZeneca R&D becoming redundant during 2012 (primarily employed in Södertälje). The information was compiled very soon after the closing of the two R&D units in Lund and Södertälje respectively, and more personnel may since then have found employment. Of the 2 105 employees in total, almost half found new employment or other

[12] Ursula Hultkvist Bengtsson, Medicon Village, Skåne (previously head of the AstraZeneca Lund site)

solution, 10 percent moved to Gothenburg, 6 percent are studying and 6 percent started their own business. There is no information available concerning the situation for about 15 percent of the personnel becoming redundant since 2010.

Manufacturing

The manufacturing unit in Södertälje is AstraZenecas largest. Four of AstraZeneca's most sold drugs are produced there and it is one of the largest pharmaceutical manufacturing units in the world. Much of the pharmaceutical export from Sweden will thus not be heavily affected by the changes made. However, some of the revenue comes from licensing within the corporation and in the longer run less R&D is likely to affect that part of the incomes. The net turnover of Swedish AstraZeneca (AstraZeneca AB) was in 2012 SEK 42bn (46 in 2011) of which 41 (45 in 2011) billion SEK were export. The licensing revenues the same year were 13.4bn SEK (13.3 in 2011).

One of AstraZenecas recent products, Brilinta (ticagrelor, with the European trade name Brilique,) was to a large extent developed in Mölndal/Gothenburg and is now manufactured in Södertälje. A positive sign of the importance of the Södertälje unit was the decision to produce Brilinta/Brilique in Södertälje during the first phases after market approval on major markets. As sales increases other manufacturing units also produces the drug. There is also a recently upgraded facility in Mölndal complying with GMP guidelines (good manufacturing practices). At the facility, drugs to be used in AstraZeneca clinical trials are manufactured.

Links to the rest of the Swedish life science industry

AstraZeneca have had few R&D collaborations with Swedish drug discovery companies leading to formal R&D agreements and only a couple of examples have been identified. At the same time the company has generated at least three company spin-offs (see Section 8.1).

It is also common with outsourcing parts of the R&D process, for example to CRO companies managing clinical trials. AstraZeneca began downsizing its Swedish operations around 2005. Since then the company has gained flexibility by using staffing companies. Interview statements estimate it to have been hundreds of staff a few years back. The demand for these services will also be reduced due to the downsizing of operations. The same goes for the demand for products and services used in laboratory research.

Links to Swedish academic research

Companies publish scientific articles for a number of reasons. In pharmaceuticals the publications adds to the credibility and legitimacy of the products, i.e. that they are linked to frontier research and affirms them being evidence based. Articles are also used as input to the regulatory process. Pharmaceutical companies have for a long time relied on close networks with academia. As the AstraZeneca Chief Executive Officer put it last year, the reasoning for networking with academia as well as other life science companies is: "*to tap into important bioscience hotspots providing more of our people with easy access to leading-edge academic and industry networks, scientific talent and valuable partnering opportunities*"[13]. Also, the

[13] Pascal Soriot, Chief Executive Officer, AstraZeneca

strong incentive for publishing in academia leads to a number of co-publications between the life science industry and academia. It is always judged whether it is strategic to make the findings public or whether the information should be patented or kept within secrecy agreements. The collaboration appears in all phases of the R&D and regulatory process but the collaborative partners changes depending on the development phase. Different type of expertise is required in different development stages

A bibliometric analysis of the co-publication pattern for AstraZeneca indicated little collaboration between AstraZeneca R&D units and that R&D units often have very close and extensive collaboration with a few academic groups. The Swedish units had very extensive publications volumes in collaboration with academia compared with that of UK and US units. The collaborative partners for the Swedish units were primarily Swedish universities and the by far largest collaborative partner was Karolinska Institutet. Other frequent collaborative partners have been Lund University, Gothenburg University, Sahlgrenska Akademin and Uppsala University. The pattern shows which scientific fields are prioritised for collaboration with specific organisations, e.g. Lund University has been the primary partner in chemistry and Gothenburg University and Sahlgrenska Akademin in the cardiovascular area. The close ties to Swedish academia are also a result of several researchers at AstraZeneca having been adjunct professors at Swedish universities.

The R&D-units being kept after the reorganisation of R&D are the largest ones and also the ones with the largest scientific output. That is however unlikely to have had bearing on the decisions which were made based on other reasoning. The closed units in Sweden had activities in areas chosen for reorganization. Respiratory and inflammation was decided to be moved to Gothenburg and thus all other units in that field were closed. Neuroscience is now less prioritized after many years of not resulting in new drugs. The neuroscience decision meant that all units devoted to that area were closed and instead, a small more or less virtual unit will be working from Cambridge (UK) and Boston (US), through networks with academia and life science companies. Also, the in-house downsizing of the respiratory and inflammation fields is likely to lead to more networking in those areas as well. The new working method will put high demands on in-house capabilities not only to monitor the development in relevant areas globally and to establish appropriate collaborations but also to have the capability to integrate the resulting knowledge into the internal R&D process successfully.

Bibliometrics showed that pharmacology is the largest research area for AstraZeneca, chemistry had an increasing trend as well as cardiovascular and oncology research, whereas there has been a decline in publications in biochemistry and molecular biology.

AstraZeneca has announced its intention to continue the collaboration with Swedish academia, especially Karolinska Institutet and the Science for Life Laboratory (a national research infrastructure located in Stockholm and Uppsala). AstraZeneca and the Karolinska Institutet have for instance together created an Integrated Translational Research Centre for cardiovascular and metabolic disease and regenerative medicine located at Karolinska Institutet's site in Stockholm, Sweden. The Centre will be set up to conduct preclinical and clinical studies aimed at advancing the understanding of cardiovascular and metabolic disease pathophysiology and assessing new drug targets for AstraZeneca's biotech units. AstraZeneca and the Karolinska

Institutet have previously (2012) announced a three-year research agreement to deliver new imaging tools that can help transition molecules through AstraZeneca's early research and development pipeline. There is also on-going collaboration with Chalmers, Gothenburg University and Sahlgrenska Akademien. Chalmers for instance collaborate with AstraZeneca also in areas outside drug discovery and development, such as material science, production technology, signal processing and medical imaging.

It is too early to tell whether Swedish universities will weaken its links to AstraZeneca due to the closing of the Lund and Södertälje units. If that happens it will reduce the investments in R&D benefitting the universities but perhaps more importantly, it will mean less knowledge and experience in academia concerning industrial R&D processes. According to AstraZeneca there were about 200 agreements of different size and content between the company and Swedish universities in 2011. Karolinska Institutet and Gotheburg University had the most agreements followed by the universities of Uppsala and Lund.

AstraZeneca is also part of a number of projects and centres co-funded by VINNOVA. Such as the VINN Excellence Centers receiving up to SEK 70m for a ten year period or the Berzelii Centers receiving up to SEK 50m from the Swedish Research Council and VINNOVA each, also for a ten year period[14]. The centers with AstraZeneca co-funding for example include; Center for Supramolecular Biomaterials - Structure dynamics and properties, Center for Protein Technology, Uppsala Berzelii Technology Centre for Neurodiagnostics, Stockholm Brain Institute and Exselent – Extremely Selective and Enantio-selective Nanoporous Materials for Controlled Sorption and Catalysis.

Links to university education

To secure competence supply it is common that large companies get involved in, and collaborate with universities concerning education. It may include everything from discussions regarding future needs of competences, receiving and supervising master and graduate students, financing of graduate students or other contributions to the education, study visits, commissioned education for employees and lecturing at university courses etc. AstraZeneca has collaborated with several universities concerning education, including many of the above mentioned ways to contribute. Examples include toxicology at Karolinska Institutet and biomedical sciences and veterinary public health at the Swedish University of Agricultural Sciences in Uppsala[15].

The possibility to have a link to industry during the education has been attractive to students and previously many finishing such educations were later recruited by AstraZeneca. Some of the AstraZeneca R&D-personnel have kept their close ties to their old academic institution which has also aided the knowledge exchange between academia and the company.

[14] http://www.vinnova.se/sv/Aktuellt--publicerat/Publikationer/Produkter/First-Evaluation-of-the-second-third-and-fourth-Round-of-VINNOVA-VINN-Excellence-Centres/, http://www.vinnova.se/sv/Aktuellt--publicerat/Publikationer/Produkter/First-Evaluation-of-the-BERZELII-CENTRA-PROGRAMME-and-its-centres-EXSELENT-UCFB-Uppsala-Berzelii--SBI-Berzelii/

[15] Source: UppsalaBIO

Beyond 2013

Beyond 2013 it is likely that the changes made by AstraZeneca in Sweden will lead to some effect on pharmaceutical exports concerning licensing, the company's' R&D-investments will be reduced by about a third[16] and the number of employees will be reduced by more than 2000 compared to 2009. All together the harsher conditions on the life science labour market might lead to changed attitudes towards a life science career. A potentially weakened link between industry and academia may also harm the mutual exchange of knowledge between the two sectors. At the same time there are positive signs, like for instance the recent extensive agreements between AstraZeneca and Karolinska Institutet. Many AstraZeneca alumni are likely to become employed in other parts of the life science industry bringing their experiences from working in R&D in a Big Pharma company with them. The trends in the life science industry are however different compared to when Pharmacia was restructured (see Section 8.2).

AstraZeneca has also launched other initiatives in Sweden in recent years, apart from the already mention R&D collaboration with for example Karolinska institutet. One such initiative is the BioHub in Mölndal, Gothenburg. AstraZenecea is expecting about 100 external employees to be housed on the site within two years. The intended tenants are primarily early-stage and growing firms engaged in innovative drug discovery and development but also other segments of the life science industry and possibly even broader than life science. They will be provided with high-end laboratory and office facilities as well as access to restaurants, meeting rooms and conference facilities. Firms will be able to rent highly specialised technical equipment and services. The intent is also that the tenants will to some extent be able to access the competence pool of AstraZeneca. Similar BioHubs have already been established at the Alderly Park site in Cheshire UK and at the site in Boston US. The Gothenburg BioHub is planned to house 15-20 companies and is intended not to compete with established incubators but aim for later stage companies.

3.3 Other large companies and corporate groups

In Figure 11 the 21 companies or corporate groups with more than 250 employees in Sweden in 2012 are listed[17]. Together they employed 49 percent of the life science industry (20 097 employees, or 13 865 excluding AstraZeneca). In 2008, the corresponding proportion was 51 percent. The data for a corporate group includes companies that have been acquired and their employees are also merged into the corporate group for the years prior to acquisition. Thus for example Dentsply includes the Astra Tech figures for earlier years. AstraZeneca in 2012 employed 15 percent of the employees in the life science industry compared to 19 percent in 2008. The other large companies have during the same period increased their proportion of the life science employees from 31 to 34 percent. The total number of employees in those companies has been constant during the period at the same time as AstraZeneca has reduced the number of employees by almost 2 200.

[16] About 1.5 BSEK meaning a reduction of about 2 percent of the total R&D-investments by the enterprise sector in Sweden. This is based on the approximation that AstraZeneca contributed about 70 percent of the total R&D-investments by the pharmaceutical industry which amounted to about 8 BSEK in 2009.
[17] Using the names they had in 2012

The number of large companies and corporate groups has ranged between 15 and 23, 1998-2012. The increase is largely due to divestments from previous Pharmacia[18] (see also Chapter 8.2). Some exceptions from this include Elekta, Hemocue and Mölnlycke Health Care having grown to more than 250 employees. Most of the other large companies have been large during the entire period, e.g. Nobel Biocare, Cambrex Karlskoga and Gambro.

Figure 9 The number of employees of AstraZeneca and other large company groups (>250 employees) compared to the total life science industry years 2008-2012

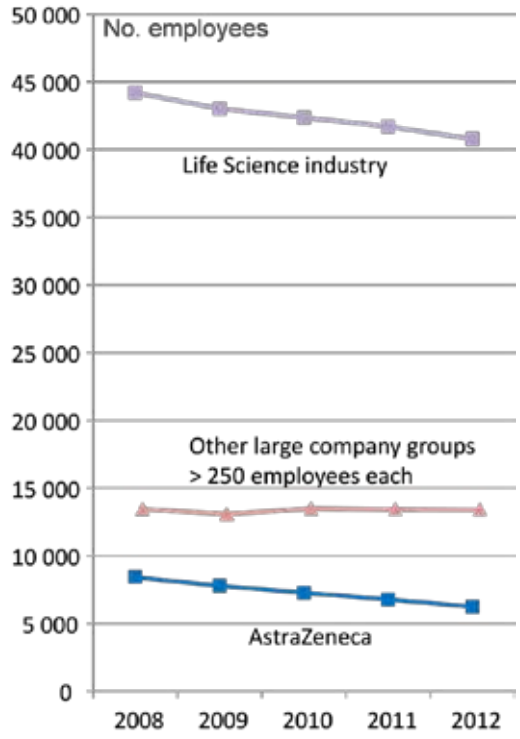
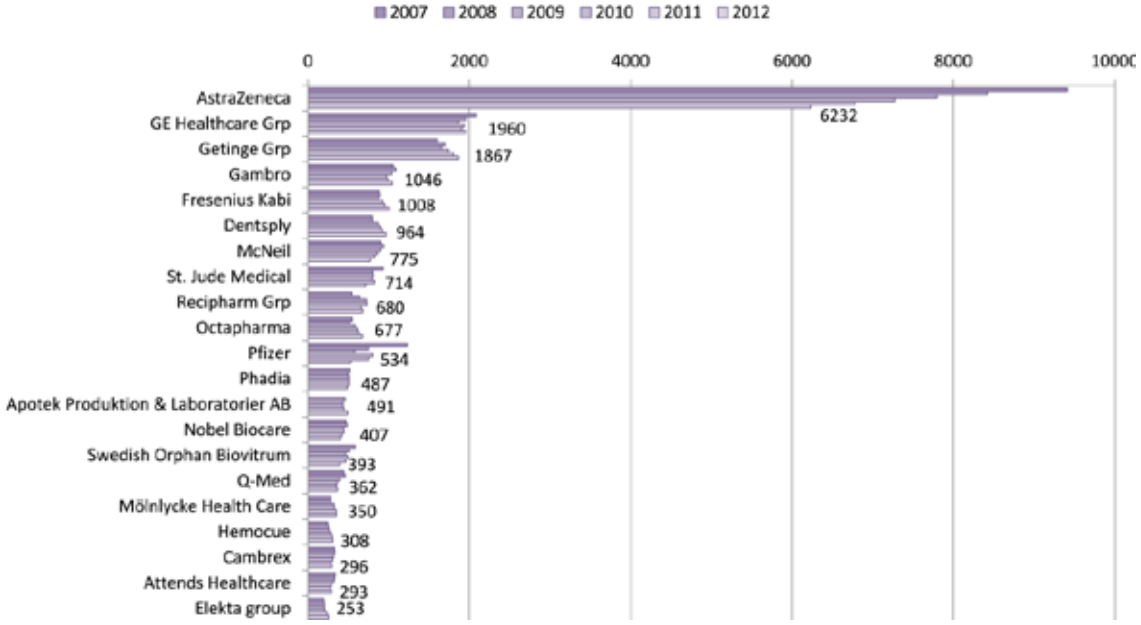


Figure 10 Number of companies or corporate groups with more than 250 employees, years 1998-2012

[18] Pfizer in this section includes Pfizer AB and Pfizer Health AB

Below the development for each of the 21 companies and corporate groups with more than 250 employees in Sweden in 2012 is shown for the years 2007-2012. There are several other companies in the Swedish life science industry which are part of globally large corporate groups but where the Swedish operations include less than 250 employees, e.g. Quintiles, Repligen, Compugroup Medical, Kemwell, Liko, Biora, Q-Med and Rechon Life Science.

Figure 11 The number of employees for each of the corporate groups with more than 250 employees in Sweden in 2012, years 2007-2012, the number of employees year 2012 is shown [19]



As is seen in Figure 11 about half of the 21 companies or corporate groups show an increasing trend regarding the number of employees in Sweden 2007-2012 counteracting the downward trend for a few of the others. The positive development is especially clear for Getinge group, Fresenius Kabi, Dentsply and Octapharma. Getinge has however in 2013 announced that some of the manufacturing in Skåne and Halland will be moved to Poland and China respectively. Similarly, in 2011, St Jude Medical moved the pacemaker manufacturing to Malaysia. Also, Nobel Biocare will close its R&D unit in Gothenburg and focus research to the units in Switzerland, USA and Canada. Most of the others show only small changes. Most of the groups have a foreign parent company. The exceptions are Elekta, Recipharm, Getinge group, Swedish Orphan Biovitrum, Apoteket Produktion & Laboratorier and Mölnlycke Healthcare.

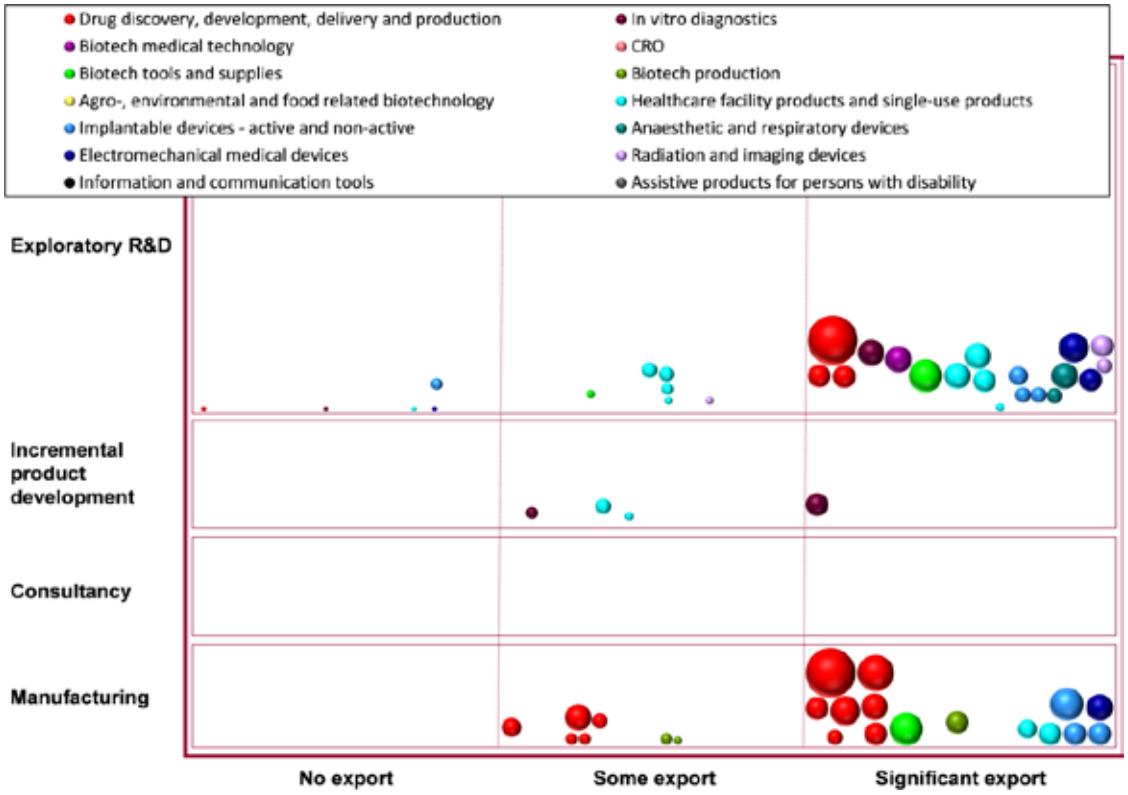
The Sectra group is no longer part of the group of large corporations in Sweden since the mammography part of the group (with 102 employees in 2012) was acquired by Philips (Netherlands) in 2012 and the rest of the Sectra operations focusing on life science do not employ more than 250 (the Sectra group in total is however, larger than 250 employees in Sweden). US Becton Dickinson also used to be one of the large life science companies in Sweden but the company has now moved the manufacturing in Skåne to India, Singapore and

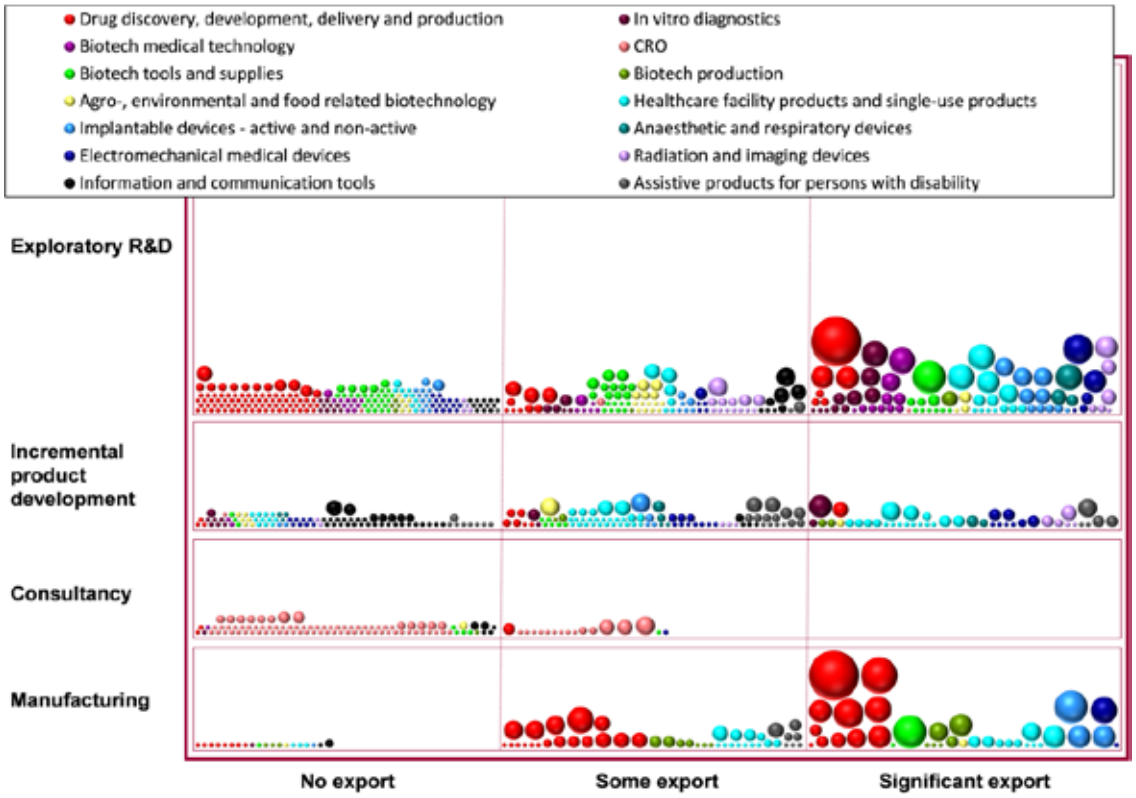
[19] The number of employees for all companies within the same corporate group in the life science industry are added in the figure, e.g. the Getinge group includes Maquet Critical Care AB, Getinge Sterilization AB, Getinge Disinfection AB, Arjo Hospital Equipment AB, Getinge Sverige AB, Getinge Infection Control AB, Arjohuntleigh AB, Getinge Skärhamn AB, Getinge AB, Arjo Scandinavia AB, Getinge International AB

Mexico. Other companies continuing activities in Sweden but no longer having more than 250 employees for instance include two companies in agrobiotechnology, Lantmännen Sw Seed and Syngenta Seeds, the CRO company Quintiles as well as the drug production company previously known under the name Ferring, now Chinese Rechon Life Science.

In the bubble diagram below, companies or corporate groups with more than 250 employees in 2012 involved in different activities have been separated so that the employees are allocated to the proper types of activities in the bubble diagram (vertical axis)

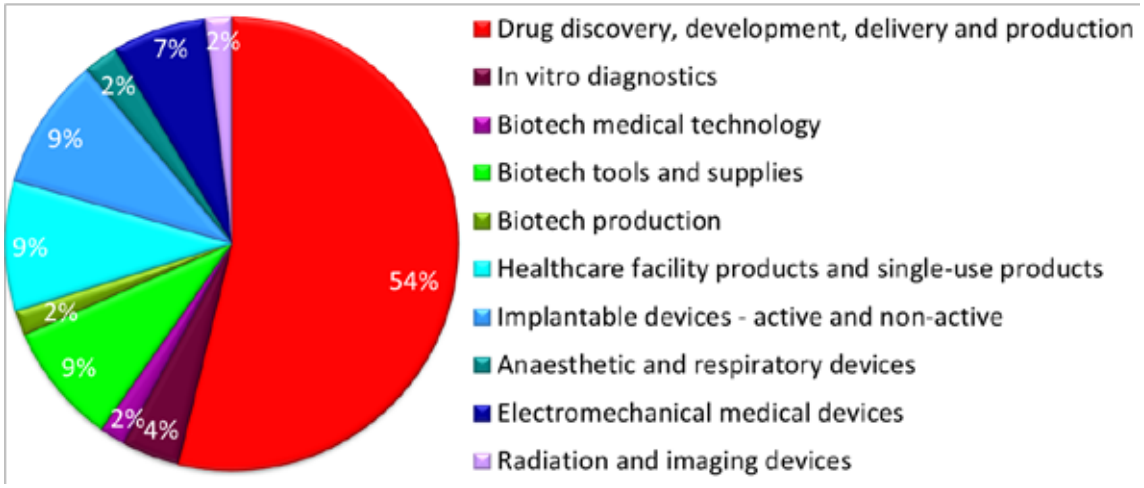
Figure 12 Bubble diagrams showing the large companies and corporate groups (top) and the total life science industry (bottom) (excluding companies in sales and marketing)





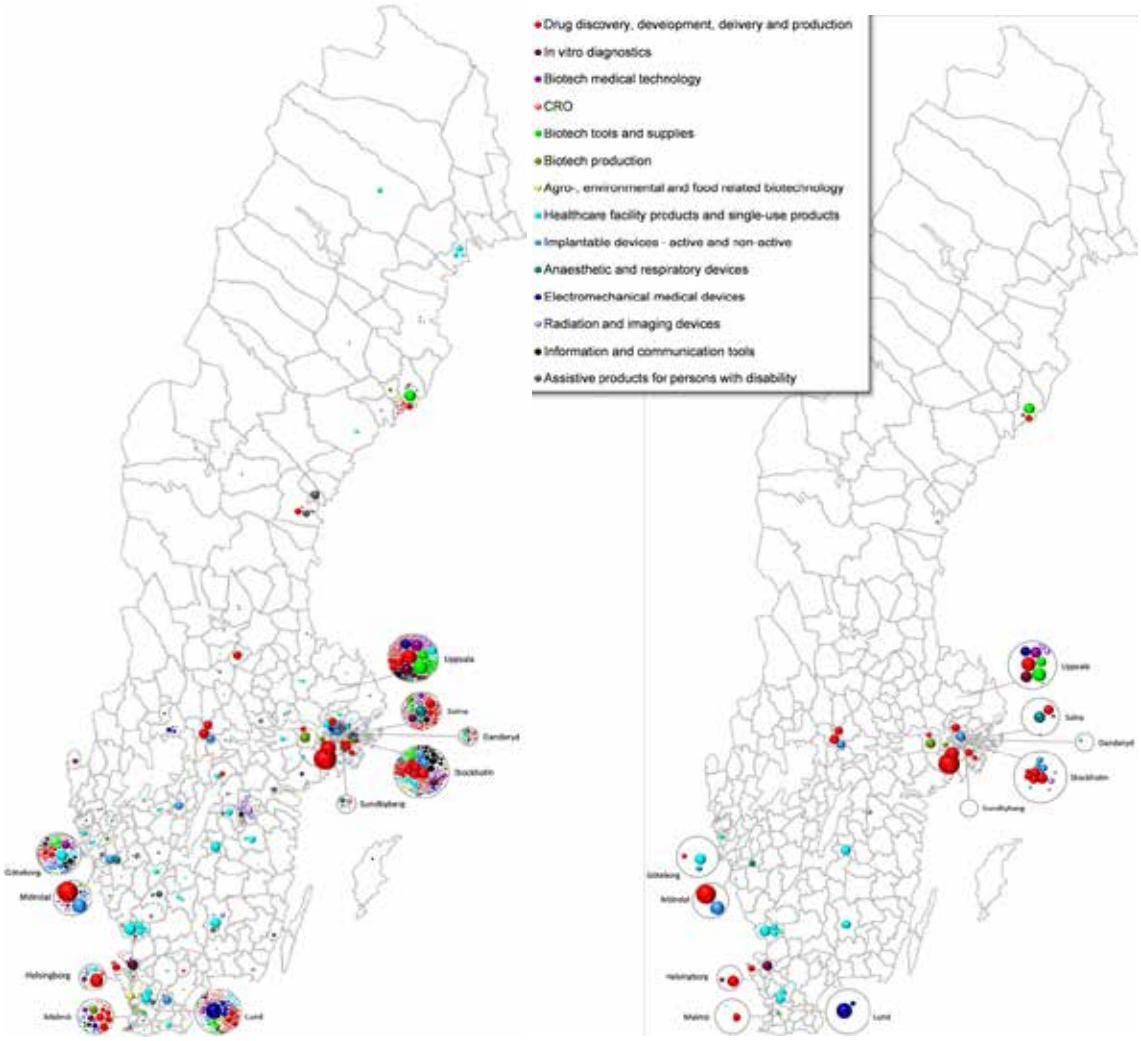
The bubble diagram shows that these large corporate groups represent most of the companies with significant export. Some of the smaller subsidiaries in the groups do not have any registered exports. It is also clear that most of the larger business segments include a few big companies which have major impact on the size of that business segment. This is particularly applicable to drug discovery, development, delivery and production, electromechanical medical devices, healthcare facility products and biotech tools and supplies. Of the large companies and corporate groups more than half of the employment is in the drugs segment, followed by 9 percent each for healthcare facility products, implantable devices and biotech tools and supplies.

Figure 13 The proportion of employees of the business segments of large companies and corporate groups in 2012 (20 097 employees in total)



As seen in the maps below, the large companies and corporate groups in 2012 have several business units across the country.

Figure 14 Geographic distribution of the large companies and corporate groups (right) compared to the total life science industry (left) [bubble size proportional to the number of employees for each company establishment and the colour represents the business segment]



Companies in the Getinge Group are primarily found in Halland but also have units in areas like Skåne, Stockholm and Västra Götaland. For the GE Healthcare Group[20], most of the employees are found in Uppsala but the group also has sites in such cities as Umeå, Lund, Stockholm and Gothenburg. Research and development is conducted in Uppsala whilst production is in Uppsala, Umeå and Skåne. Pfizer has its production activity in Strängnäs and its sales and marketing activity in Stockholm.

[20] Including GE Healthcare BioSciences, Uppsala Imanet, Biacore, GEMS PET Systems and Breas Medical

A few companies also have activities outside the regions in which the bulk of the life science industry is clustered. These for example include production units of Nobel Biocare, Recipharm and Cambrex in Karlskoga, Attends Healthcare in Aneby and Getinge Disinfection in Växjö.

In the next section (Section 3.4) the companies belonging to the above described large corporate groups are excluded even if individual companies have less than 250 employees.

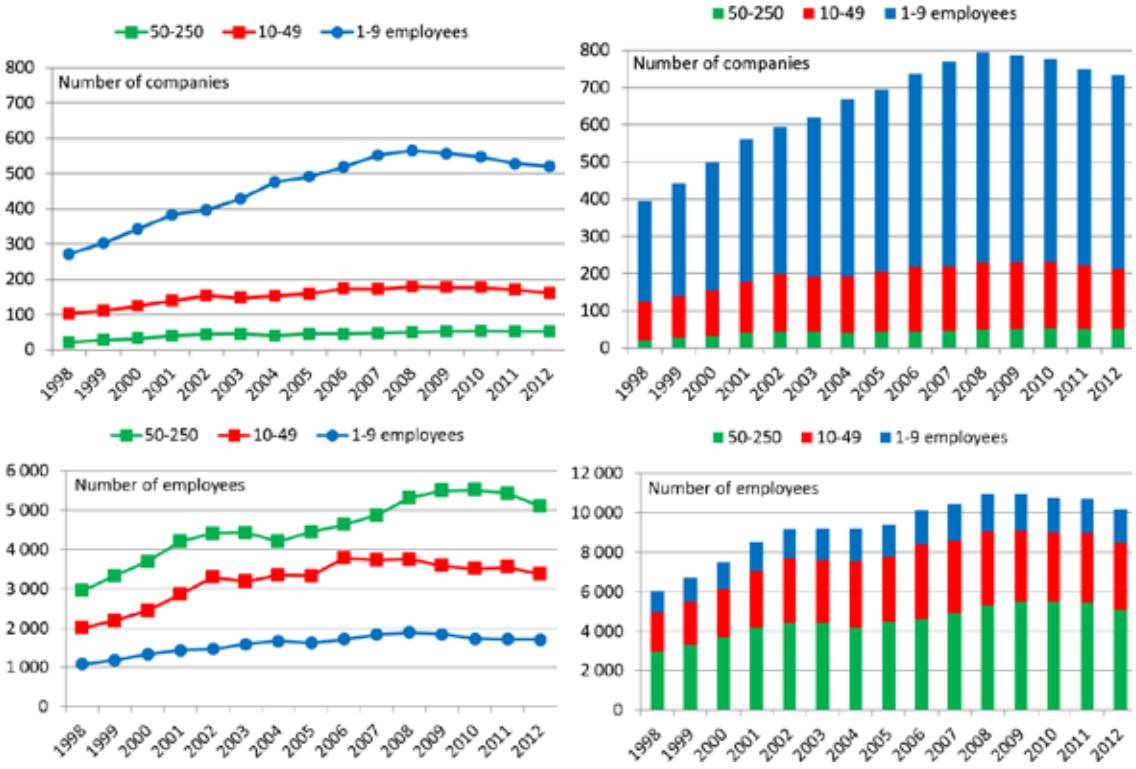
3.4 Micro-, small- and medium-sized companies

The SMEs (1-250 employees) have in the following figures been divided into size classes by number of employees for each year from 1998-2012. The companies identified as part of the large corporate groups described in the previous section (Section 3.3) have been excluded from the analysis of the SMEs in the present section. For instance Recipharm, Getinge or GE Healthcare subsidiaries are thus not included in Figure 15 to Figure 17.

The number of companies divided into size as well as the development of the number of employees for the companies belonging to the size classes is shown in Figure 15. As was previously mentioned the number of large companies has shown little variation during the time period. The same goes for the size class 50-250 employees (middle sized). After a slight increase until 2002, the number has varied between 45-52 companies each year. The increase of the number of companies in size class 10-49 (small sized) levelled off in 2006 and there has been a slight decrease in the last couple of years.

The figure illustrates the clear trend towards a dramatic increase in the number of micro-sized companies until the number of companies peaked in 2008, at 565 micro sized companies. The decline since 2008 has resulted in the number of companies with less than 10 employees becoming 520, and the employment in the size class declining slightly. Since the development of the number of employees per size class follows the number companies, the medium size class grew until 2008 and the small size class started to slightly decline in 2007.

Figure 15 The number of micro-, small- and medium-sized companies and their employment years 1998-2012 (excluding companies which are part of large corporate groups) [left: separate lines, right: cumulative bars]



The conclusion, especially in recent years, is that few of micro-sized companies reach beyond the micro-sized segment. Similarly, small and medium-sized companies have shown no average growth in recent years. Thus the companies mostly grew in the beginning of the studied time period. At the same time new enterprises have been formed, the absolute majority being university spin-offs. There are a number of reasons for so few of the micro companies not growing, for example too little technical and commercial verification before starting the company, difficulties in finding financing and no ambition to grow are some plausible reasons. The down-turn in number of micro-sized companies may also have some connection to a number of companies choosing to outsource all functions and keeping the project company virtual.

Size classes and business segments

The columns in Figure 16 below show different aspects of the development of the business segments for each size of class (medium, small and micro): number of companies; number of employees 1998-2012 as well as proportions of the employees and number of companies in 2012 in the circle diagrams.

Micro-sized companies: The dynamics is largest in this size class with many companies starting and stopping employing every year. For example, in 2012, 62 companies stopped employing and 47 started employing into this size class compared to 2011. At the same time 16 companies previously in a larger size class reduced its number of employees to enter the micro-sized class

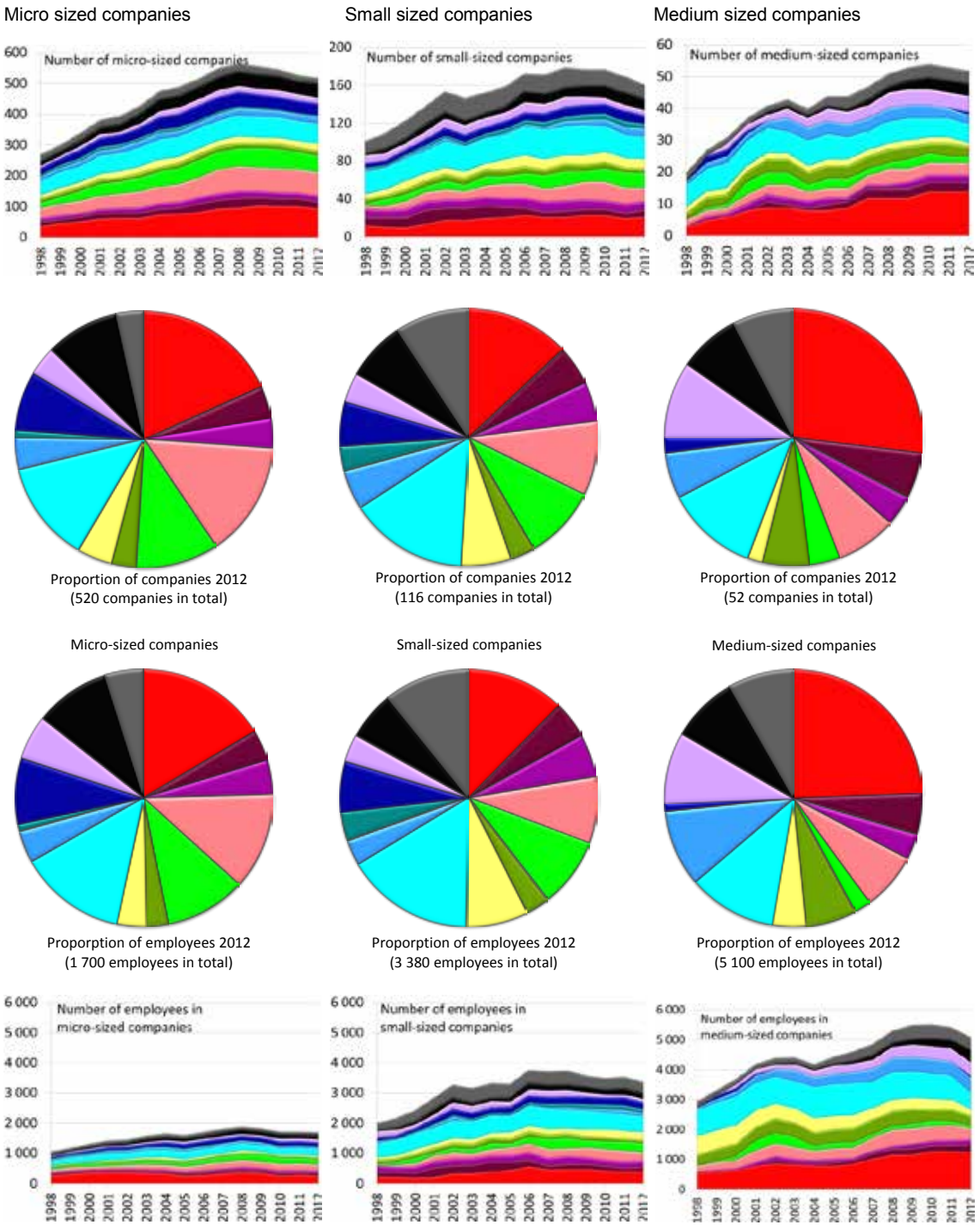
and 13 increased their number of employees to move up from micro-sized, i.e. generating a net decrease by 12 micro-sized companies. Over the entire time period the increase in number of micro-sized companies has been particularly drastic in the drugs segment, for CROs and ICT-tools. In relative terms also radiation and imaging devices and biotech medical technology have significantly increased the number of companies.

Small-sized companies: Among the small sized companies, contrary to all other size classes, the drug business segment is not the largest neither in terms of companies nor employees, instead healthcare facility products is the largest segment on both accounts. CROs and biotech tools are the segments increasing the number of companies most, i.e. companies are moving up from the micro-sized class. Those segments also show the by far largest increase in employment, about 250 and 260 employees respectively. Also, the business segments agro-, environmental and food related biotechnology; drugs; ICT tools and assistive products for persons with disability showed a significant increase, ranging between 140 and 180 employees each.

Medium-sized companies: The only significant change in terms of number of companies is the increase by 11 companies in the drugs business segment. Thus companies have been moving up from the small-sized segment. This is also the segment with the largest increase in employment, 670 personnel, largely explained by drug production companies such as Kemwell (previously Pharmacia), Ccs Healthcare, Qpharma, Carmel Pharma (which however will cease its Swedish activities after being acquired by Becton Dickinson and later closed) and Unimedic as well as companies in reformulation and re-indication such as Meda and Orexo. The downsizing of Syngenta Seeds and Lantmännen Sw Seed causes a drastic decrease in number of employees for the segment agro-, environmental and food related biotechnology. The drastic decrease for healthcare facility products is largely due to the manufacturing unit of Becton Dickinson leaving Sweden counteracting the growth of Liko and also AMO Uppsala (previously Pharmacia) entering the size class after being divested from Pfizer in 2004[21].

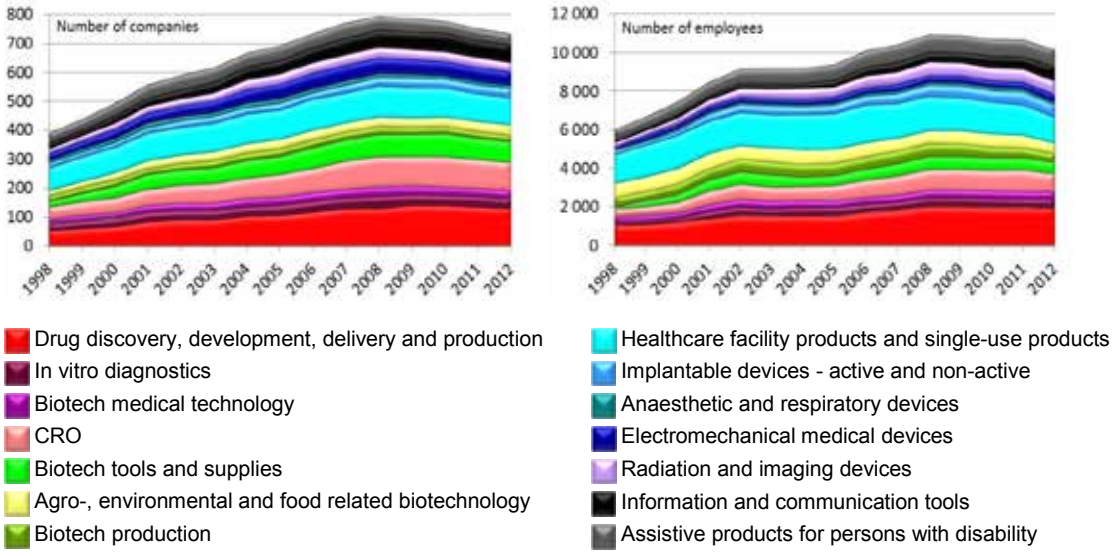
[21] Pfizer acquired Pharmacia Corporation in 2003

Figure 16 The number of micro-, small- and medium-sized companies and their employment years 1998-2012 as well as the corresponding proportions in the business segments in 2012 (excluding companies which are part of the large corporate groups described in Section 3.3



In Figure 17, the development of number of companies and employees for different business segments for the entire group of micro-, small- and medium-sized companies is shown when excluding the companies that are part of large corporate groups. Looking at the specifics of different business segments, the largest increases in numbers of companies are seen for drug discovery and development, biotech tools and supplies, CROs and electromechanical medical devices. The average number of employees in the population has been constant or increased for 12 of the 14 business segments. The exceptions are drug discovery, development, delivery and production and agro-, environmental end food related biotechnology. For the first segment the explanation partly lies in the continuous forming of new companies staying micro-sized, whereas the explanation for the latter primarily is a drastic decrease for two rather large companies in the medium-sized class during the period.

Figure 17 The number of micro-, small- and medium-sized companies and their employment, years 1998-2012 (excluding companies which are part of the large corporate groups described in Section 3.3)



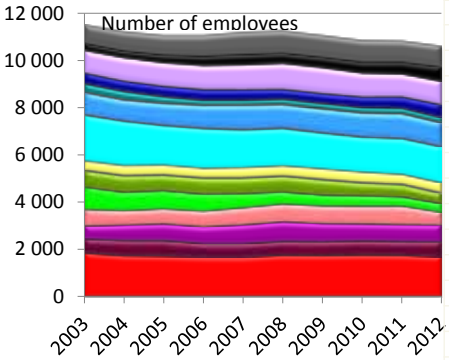
There has been a steep relative increase in the number of companies in ICT tools, drug discovery, development, delivery and production, CROs and biotech tools and supplies. The business segment, ICT tools, is also one of the segments with the most drastic relative increase in the number of employees. A number of medical technology business segments have also clearly increased their average number of employees due to a relatively slow entry of new companies at the same time as there has been an average growth of the already established companies. This for instance includes implantable devices, anaesthetic and respiratory devices, radiation and imaging devices, ICT tools and assistive products for persons with disability. In absolute numbers however, the drugs segment has grown the most, with about 860 employees.

Monitoring the development of the SME population present in 2003

In Figure 18 the SME population in 2003 is monitored 2003-2012 resulting in a decrease by 524 employees. Identifying the companies responsible for the decline however reveals that the majority of the employees stayed in the Swedish life science industry. Biacore (biotech tools

and supplies) as well as Instrumentarium (anaesthetic devices) with almost 200 employees in 2003 each, were both acquired by GE Healthcare, Ferring (drugs, 180 employees in 2005) is now Rechon Life Science, a company formed after 2003 and Cresco Ti System (implants, 17 employees) is part of Dentsply. Thus much of the decrease in employment in the population is explained by acquisitions by companies outside the SME population of 2003 but belonging to the Swedish life science industry.

Figure 18 Monitoring the number of employees in the 2003 SME population years 2003-2012



Absolute change	Relative change [%]	
107	14	Assistive products for persons with disability
305	93	Information and communication tools
42	4	Radiation and imaging devices
86	18	Electromechanical medical devices
-146	-41	Anaesthetic and respiratory devices
69	7	Implantable devices - active and non-active
-412	-21	Healthcare facility products and single-use products
8	2	Agro-, environmental and food related biotechnology
-264	-38	Biotech production
-547	-59	Biotech tools and supplies
-165	-23	CRO
150	27	Biotech medical technology
49	8	In vitro diagnostics
-160	-9	Drug discovery, development, delivery and production
-524	**-5**	Total

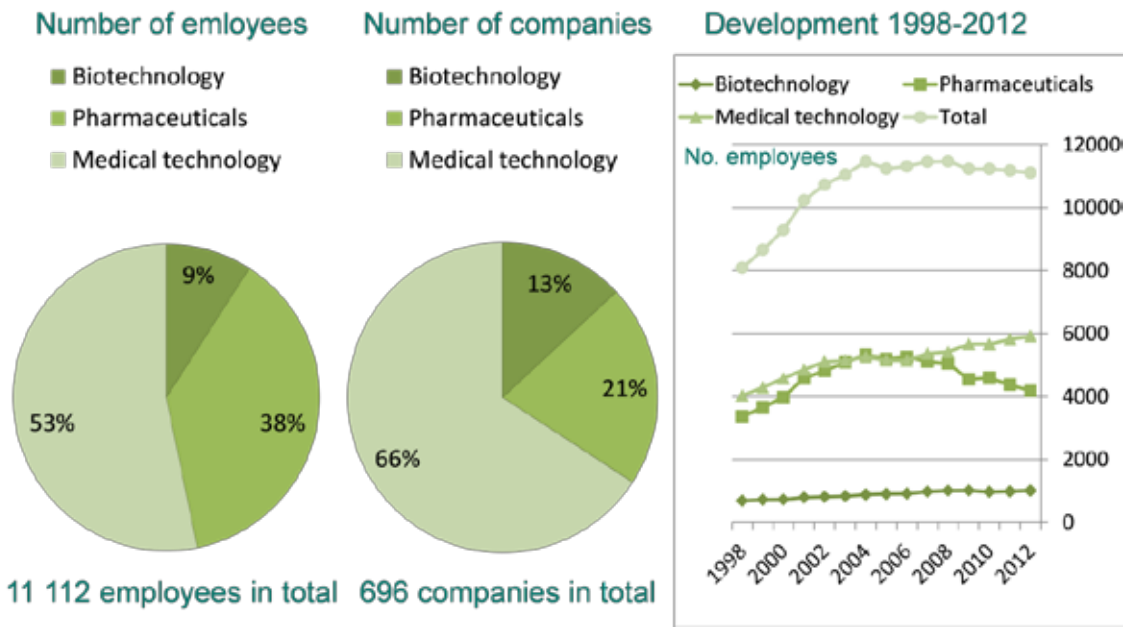
There is however several companies ceasing employing or going out of business. Most of those companies did however not have that many employees, with Kaltoplast with 63 employees in 2003 closed by its owner Nolato AB and Viranative with 39 employees in 2003 as two exceptions. Smaller companies include Dilab, Gnothis and Quiatech which have gone out of business and companies such as Medipharm (part of the food corporation Arla), Q-sense, Bactus, Orasolv, Melerit, PGL Professional Genetics Laboratory, Bioagri, Sidec, Midorion and Layerlab have all ceased employing. One example of a foreign acquisition leading to an immediate closing of Swedish operations was Global Genomics acquired by Genizon BioSciences in 2005. About half of the downsizing of biotech production is the already mentioned closing of the DSM Anti-infectives site in Strängnäs.

The companies growing to become large companies in the 2003 SME population are Hemocue, Elekta, Octapharma, Q-Med and St. Jude Medical Systems. A number of companies have grown but stayed under 250 employees, e.g. in the ICT tools area (e.g. Cambio Healthcare) and In vitro diagnostics (e.g. Cepheid).

3.5 Companies involved in sales and marketing in Sweden

There are almost 700 companies with employees in Sweden involved in sales and marketing of biotechnology, pharmaceutical or medical technology products but without manufacturing or R&D in Sweden. Included in this group are companies that besides sales and marketing are involved in setting up clinical trials in Sweden.

Figure 19 Distribution of the companies and employees involved in sales and marketing in Sweden into biotechnology, pharmaceuticals and medical technology



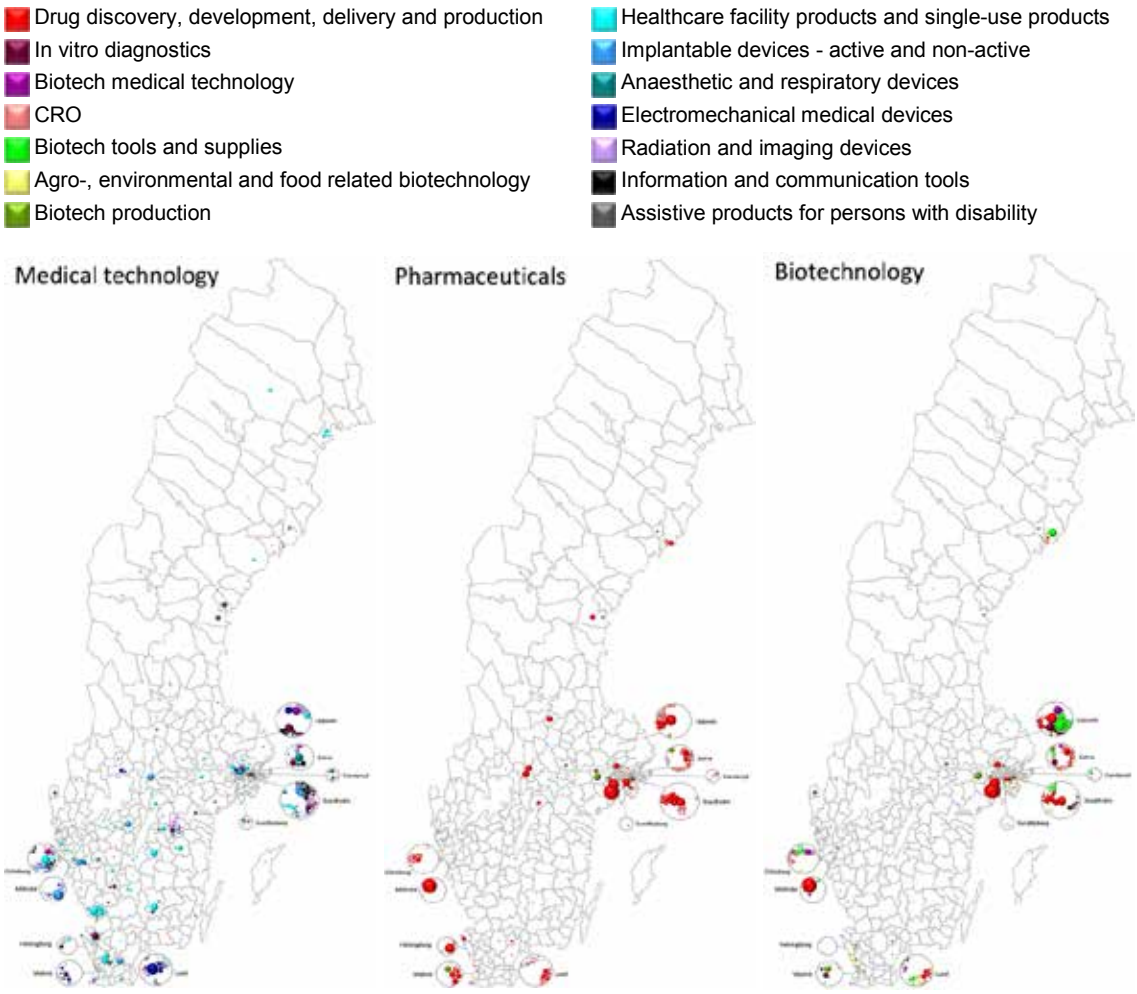
The number of employees were about 11 100 in 2012, which corresponds to 27 percent of the life science industry employees. The development has been almost flat in recent years with a very slight decrease. The increase years 1998-2004 should be interpreted with some caution since the company population during that time period may lack some companies. Medical technology has by far the largest number of companies (66 percent) and also about 53 percent of the employees in 2012, followed by pharmaceuticals, 21 percent of the companies and 38 percent of the employees. The pharmaceutical companies have reduced their sales and marketing units both regarding the sales function and the expertise in clinical trials. According to a survey by LIF the number of employees working with clinical trials has almost decreased by 50 percent years 2006 to 2012. The increased focus on outsourcing to CROs has meant less need for in-house personnel and thus more flexibility for the Big Pharma companies. At the same time this risks resulting in less direct contact between clinical practice and the development processes in industry.Another explanation for a reduced number of employees in pharmaceuticals may be that the companies have chosen to reduce the number of clinical trials in Sweden.

The tasks of the facilities of global pharmaceutical companies in Sweden include several other functions than sales and marketing. Functions for instance include: the monitoring of side effects; managing local R&D projects; collaboration with quality registers, Swedish authorities and counties; scientific advisory boards; regulatory and marketing issues; communication issues such as those with patient associations, websites (e-health), media etc.; involvement in health economics/outcomes research; price and reimbursement processes; as well as involvement in, and managing of clinical trials.

4 Medical technology, pharmaceuticals and biotechnology

In the following sections the size, development, exports and other aspects of the medical technology, pharmaceuticals and biotechnology sectors will be described. In Figure 20 below, the geographic distribution of company facilities of the three sectors are visualised.

Figure 20 Geographic distribution of company facilities in medical technology, pharmaceuticals and biotechnology



Geographically, the medical technology sector is the most dispersed of the three life science sectors, generating employment in many parts of Sweden. Both the pharmaceutical and biotechnology sectors have a higher agglomeration to the regions surrounding Stockholm/

Uppsala, Skåne and Västra Götaland as well as a smaller population of companies in Umeå. In pharmaceuticals, it is primarily the manufacturing units which are found outside those regions.

4.1 Medical technology

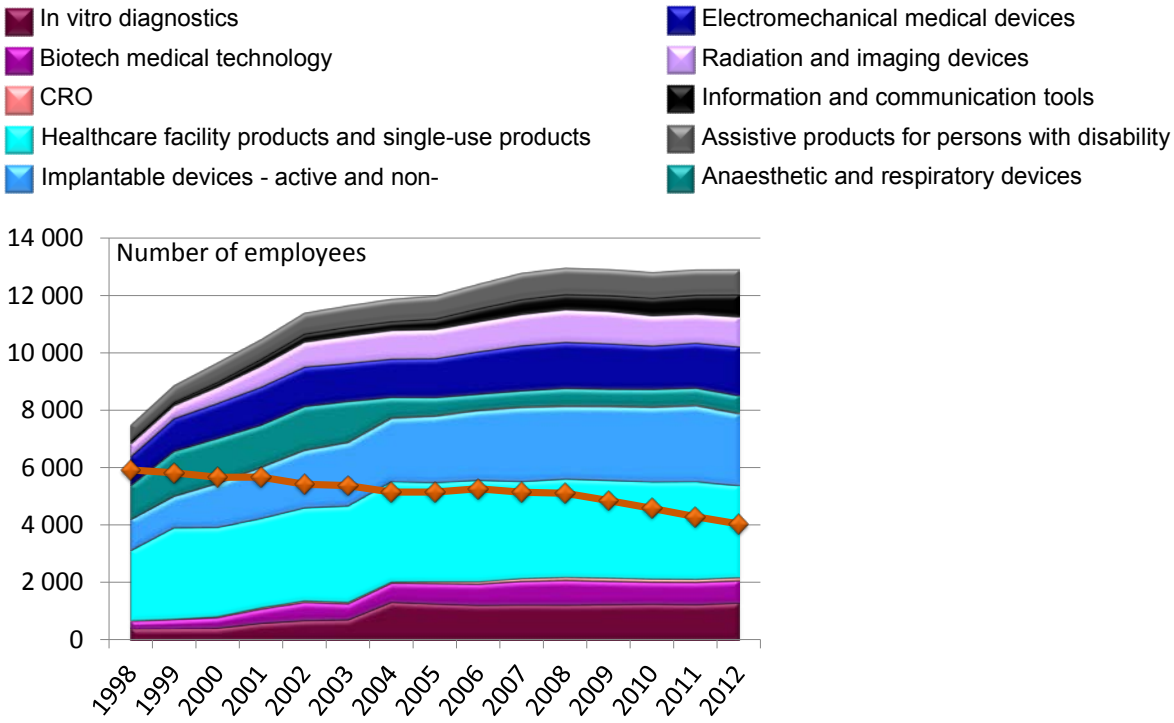
The medical technology sector employs about 16 940 people in almost 740 companies. Over 4000 are employed in sales and marketing companies. Regarding companies in R&D, consultancy and/or manufacturing, the sector is dominated by the business segments 'healthcare facility products' and 'implantable devices', jointly comprising more than 34 percent of the employment in the sector. Then follows the business segments: 'in vitro diagnostics', 'electromechanical medical devices' and 'radiation and imaging devices', with between 1 000 and 1 800 employees each.

Table 5 The size of the medical technology sector in Sweden 2012

BUSINESS SEGMENT	NO. EMPLOYEES	NO. COMPANIES
IN VITRO DIAGNOSTICS	1 278	37
BIOTECH MEDICAL TECHNOLOGY	781	30
CRO	135	22
HEALTHCARE FACILITY PRODUCTS AND SINGLE-USE PRODUCTS	3 187	110
IMPLANTABLE DEVICES - ACTIVE AND NON-ACTIVE	2 493	39
ANAESTHETIC AND RESPIRATORY DEVICES	623	12
ELECTROMECHANICAL MEDICAL DEVICES	1 712	54
RADIATION AND IMAGING DEVICES	1 035	33
INFORMATION AND COMMUNICATION TOOLS	793	64
ASSISTIVE PRODUCTS FOR PERSONS WITH DISABILITY	872	37
MARKETING AND SALES	4032	299
TOTAL	**16 941**	**737**

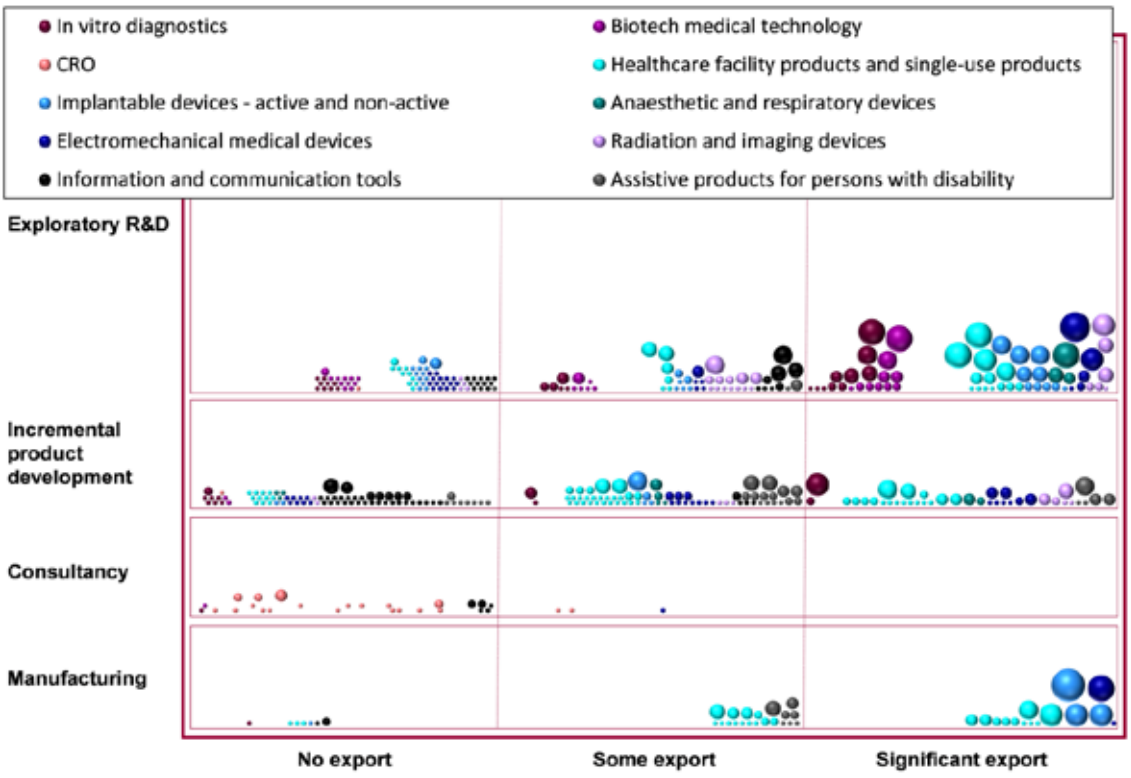
As has already been mentioned, the development of employment in Medical technology years 1998-2003 should be analysed with some caution since the assembly of the Medical technology part of the database was initiated in 2003.

Figure 21 The size of the medical technology sector in terms of employees, years 1998-2012 (orange line is companies focused on sales and marketing)



Despite companies in sales and marketing having declined by 25 percent, i.e. almost 1 340 employees, the total number of employees is almost the same in 2003 as in 2012. Companies with R&D, consultancy and/or manufacturing, have increased their employment by more than 1 240, counteracting the negative trend in the sales and marketing area. The business segment showing the steepest relative increase since 2003 is 'ICT tools', albeit from a low level, whereas 'anaesthetic and respiratory devices' is the segment with the largest relative and absolute decrease (minus 790 employees). The largest increases since 2003, in absolute numbers, include the segments 'in vitro diagnostics' (plus 556 employees), 'ICT tools' (plus 465), 'electro-mechanical medical devices' (plus 374), 'implantable devices, (plus 282) and 'biotech medical technology' (plus 226). During the latest five-year period, 'ICT tools' (plus 242) and 'electromechanical medical devices' (plus 100) had the largest increases in employment and 'healthcare facility products' the largest decline (minus 228).

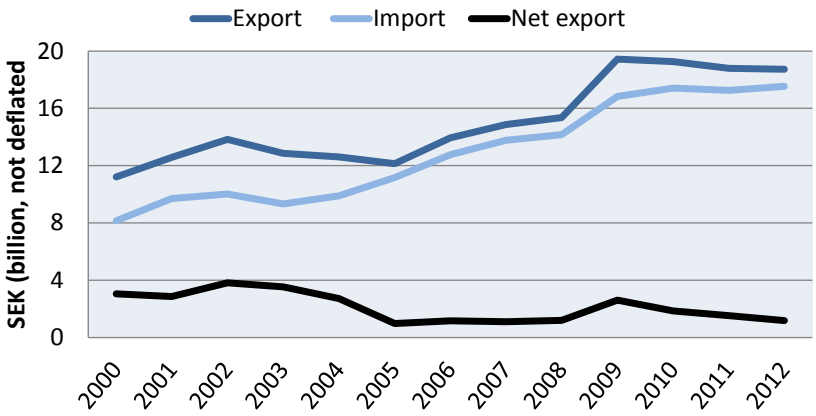
Figure 22 Bubble diagram showing medical technology companies active in R&D, consultancy or manufacturing in Sweden in 2012 [bubble size (volume) is proportional to the number of employees]



A larger proportion of medical technology companies are categorised as belonging to the "Incremental product development" activity category (42 percent) than for the two other sectors in the present study. For medical technology, the same proportion of the company population is found in "Exploratory R&D" as in "Incremental product development". Like drugs, medical technology products must undergo a regulatory process, but usually developing these types of products does not stretch over as long a time period as for drugs. Once a technical appliance is launched onto the market, the product is often subject to further development. Also, the devices often have a shorter product life cycle. Since few of the companies have more than 500 employees, they have not been divided across different activity categories. Thus, the number of employees in manufacturing in the medical technology sector is underestimated in the visualisation of Figure 22. Many of the companies with 50-500 employees do have manufacturing units in Sweden.

Of the companies with R&D, consultancy and/or manufacturing, 25 percent have significant exports and 32 percent have some export. As may be expected, it is mainly consultancies (which usually cater a local market) and the smallest companies which have no export. The companies with significant exports represent 72 percent of the employees in the medical technology sector. The medical technology export has increased by 67 percent 2000-2012, but in the last three years there has been a very slight decline.

Figure 23 Trade in medical technology 2000-2012 (SPIN: 26.600, 32.501 and 32.502)* [adjusted for drop-off, SEK billion]



Source: Statistics Sweden
** 26.600 radiation and electromedical devices; 32.501 medical and dental instruments and supplies; 32.502 dentures*

In the area of advanced medical devices the market development in recent years varies between product segments but some overall trends can be identified. The market growth has been almost flat in Northern and Western Europe, decreasing in southern Europe and still increasing steeply in Asia, especially in China, but perhaps not showing the same impressive growth in China as a few years back. A slowdown in recent years in the US is starting to change and there are positive signs again. There are a number of large global corporations, each with their own specialisations and niches, dominating the scene. Companies such as General Electric, Siemens, Philips, Medtronic, Johnson & Johnson and Baxter etc. have varying market shares in different segments forming almost oligopolistic markets. Many of the corporations with large world-wide market shares in their particular niches are present in Sweden, with R&D and/or manufacturing, such as Dentsply (previously Astra Tech), Baxter (Gambro), St Jude, Nobel Biocare, Siemens, Fresenius, Becton Dickinson, Thermo Fisher (Phadia) etc. A trend of consolidation has also contributed to the more oligopolistic markets forming in particular niches. There are examples of companies with a long tradition of R&D in Sweden, with high world-wide market shares in their niches, strengthening their R&D much more in other locations than those in Sweden.

The product life cycle is much shorter than for pharmaceuticals and the companies are often devoted to both incremental innovation and radical innovation. Incremental innovation may include new additions and improvements of established products being launched as well as including less complex versions for specific markets. Radical innovation, for instance include the combination of more than one technology in one system or going from diagnostic to therapeutic applications. The innovation processes are iterative and a prerequisite for innovation is involvement of, and collaboration with clinical practice throughout the innovation process and the complete product life cycle.

4.2 Pharmaceuticals

The pharmaceutical industry in Sweden in 2012 had 17 287 employees in 386 companies, of these, almost 3 400 were employed in 147 sales and marketing companies.

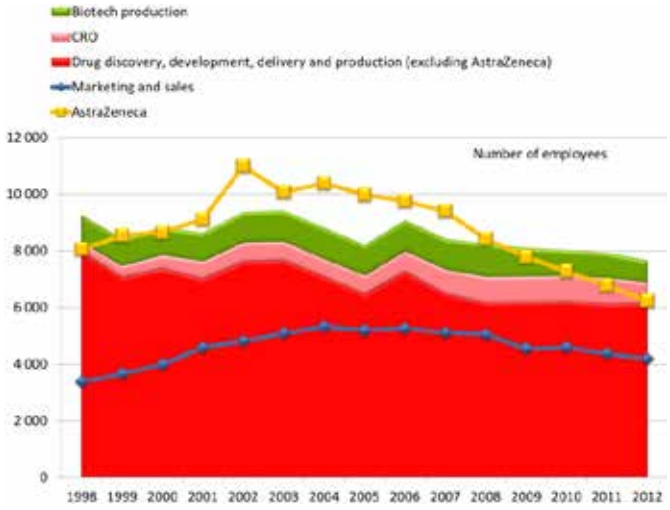
Table 6 The size of the pharmaceutical industry in Sweden 2012

BUSINESS SEGMENT	NO. EMPLOYEES	NO. COMPANIES
DRUG DISCOVERY, DEVELOPMENT, DELIVERY AND PRODUCTION (EXCLUDING ASTRAZENECA)	6167	145
ASTRAZENECA	6 232	1
CRO	735	75
BIOTECH PRODUCTION	784	18
SALES AND MARKETING	3 369	147
TOTAL	**17 287**	**386**

Companies in sales and marketing showed a slight rise in employment years 1998-2004, and since then a slight decline. The total difference during the entire period thus ended up in a net increase by more than 800 personnel even though the net decline since 2008 was more than 860.

The number pharmaceutical companies involved in R&D, consultancy and/or manufacturing peaked in 2010 with 259 companies and has since then declined to 239 companies with 13 918 employees in 2012. The peak year in terms of employees was 2002 with 20 372 employees. There has been a reduction by 6 454 employees since then. This decline is primarily due to AstraZeneca's and Pfizer's decreased number of employees. Pfizer currently has no own research facilities in Sweden. However, there is collaboration on research with Karolinska Institutet amongst others and Sweden is one core country in Europe for the companies' early clinical research. Since 2008 AstraZeneca has declined by almost 2 200 employees, the rest of the drug segment was flat. The segments 'biotech production' (including only those related to biopharmaceuticals) and CROs have both declined, minus 372 and 184 employees respectively.

Figure 24 The size of the pharmaceutical sector in terms of employees, years 1998-2012



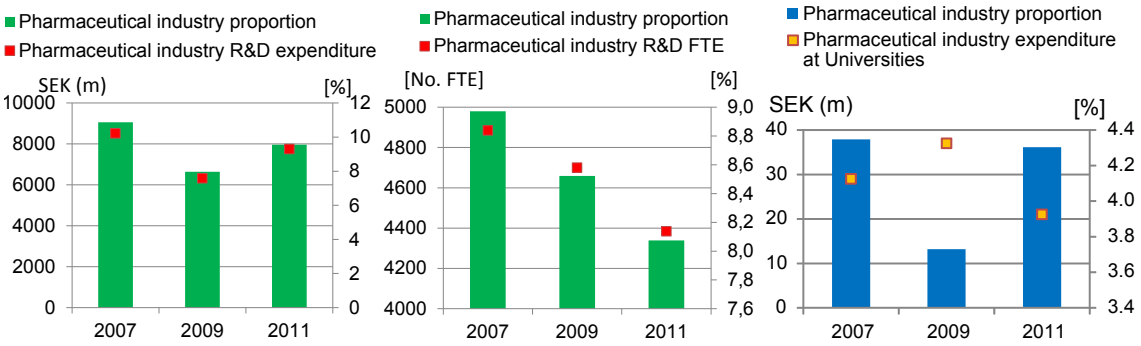
R&D-investments in Sweden

Below the R&D expenditure of the pharmaceutical industry is shown, both in absolute numbers and in relation to the total Swedish industry (with a total expenditure of SEK 81 100m). In 2011 the pharmaceutical industry invested SEK 7 752m in R&D, corresponding to 9.6 percent of the

investments of the total Swedish industry. The proportion is 1.6 percent larger than in 2009 but smaller than the proportion in 2007, 10.9 percent[22]. It is likely that the closing of the R&D unit of AstraZeneca in Lund has not yet affected the figures completely and the corresponding closing of the Södertälje unit not at all.

The pharmaceutical industry in Sweden spends 11.6 percent of the net turnover on R&D and 35.4 percent of employees are, according to Statistics Sweden, R&D personnel (not only PhDs). The corresponding proportions for the computers, electronics and optics as well as the automotive industries are 13.6/32.4 and 5.5/12.4, respectively. The number of R&D personnel has declined from 9.0 percent to 8.1 percent of the total R&D personnel in Swedish industry between 2009 and 2011.

Figure 25 R&D expenditure (first panel), number of R&D personnel (second panel) and expenditure on outsourced R&D at Swedish universities (third panel) of the pharmaceutical industry in Sweden in absolute numbers and in relation to the total for Swedish industry

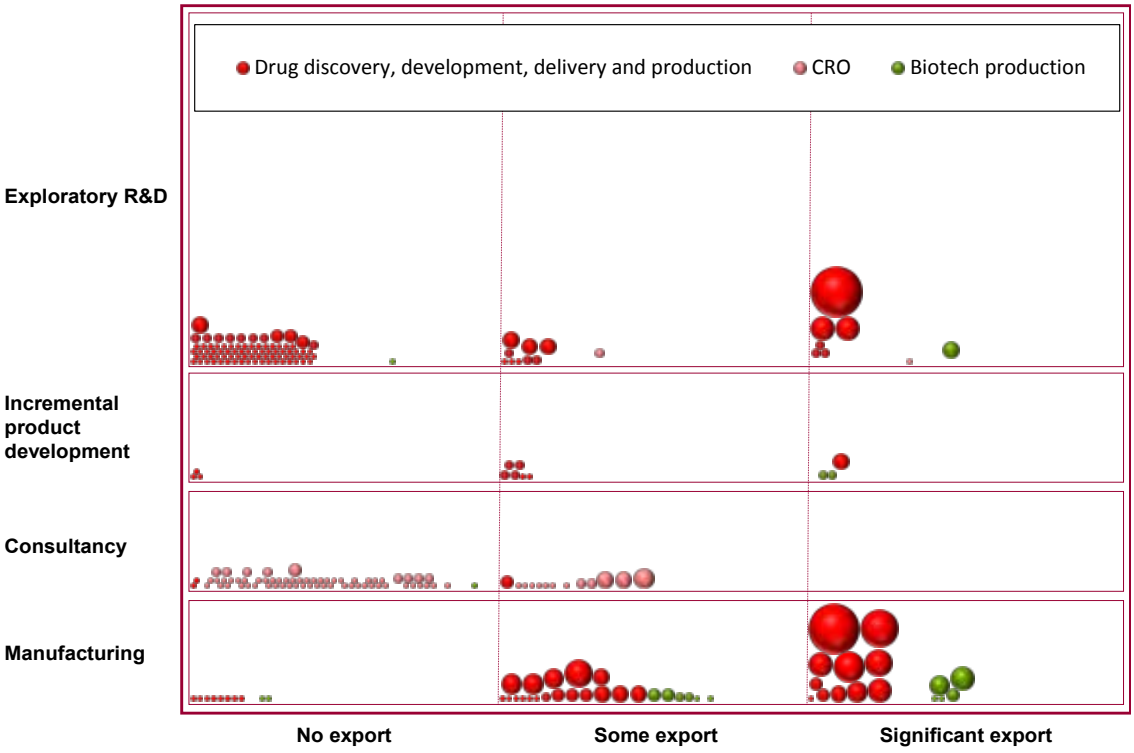


Statistics Sweden

In addition to investments in own R&D, companies also outsource R&D to universities, receiving SEK 21m in 2011. This investment corresponds to 4.3 percent of the total R&D expenditure at Swedish universities by Swedish industry.

[22] The financial crisis is likely to have affected the results for 2009

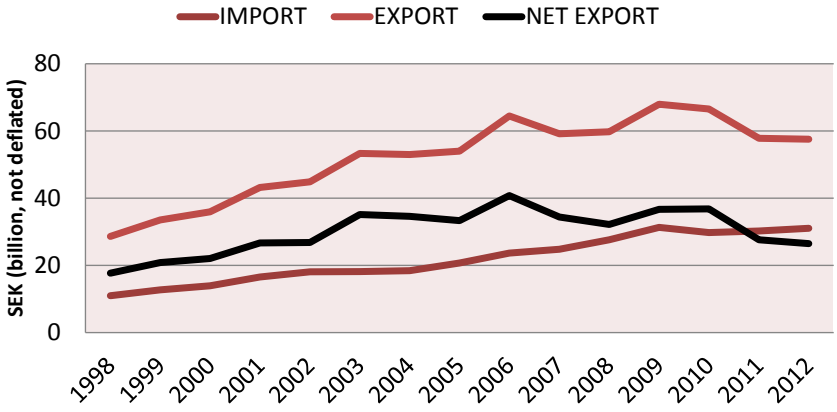
Figure 26 Bubble diagram showing pharmaceutical companies active in R&D, consultancy or manufacturing in Sweden in 2012 [bubble size (volume) is proportional to the number of employees]



The proportion of pharmaceutical companies categorised as belonging to the "Exploratory research" activity category is 42 percent, 32 percent in consultancy, but only five percent are found in "Incremental product development". The drugs segment includes several contract manufacturing organisations, such as the Recipharm group of companies. This together with the manufacturing sites of some of the large companies (e.g. AstraZeneca, McNeil, Octapharma and Fresenius Kabi) contributes to the many red manufacturing bubbles seen in the bubble diagram. This segment also includes a large number of small academic spin off companies with exploratory research and a significant number of CROs in the consultancy activity category.

Of the companies with R&D, consultancy and/or manufacturing, eight percent have significant exports and 25 percent have some export. As may be expected, it is again mainly consultancies and the smallest companies which have no export. Since those companies are a very large proportion of the total population, as much as 57 percent of the companies have no export. At the same time the 'no export' companies only represent 904 employees (6 percent). The companies with significant exports however represent 76 percent of the employees in the pharmaceutical sector. The pharmaceutical export has increased by 89 percent 2000-2012, but has experienced a significant downturn since the peak year in 2009. The export in 2009 was SEK 68bn and had in 2012 declined by SEK 10bn, to SEK 58bn.

Figure 27 Trade in pharmaceuticals* 1998-2012 [adjusted for drop-off, billion SEK]



Source: Statistics Sweden
** SITC, Standard International Trade Classification codes: 541 and 542*

In 2012 AstraZeneca AB accounted for SEK 41bn of the pharmaceutical export (SEK 45bn in 2011), i.e. about 71 percent of the Swedish total. According to AstraZeneca AB, the licensing revenues in 2012 were SEK 13.4bn (13.3bn in 2011). About 30 percent of AstraZeneca sales are generated from products manufactured in Södertälje. The reasons for the downturn are not known.

As for medical technology products, pharmaceuticals proved not to be a product group sensitive to the effects of the financial crisis in terms of export. The export of many other products contributing largely to Swedish exports declined steeply in 2009[23].

4.3 Biotechnology

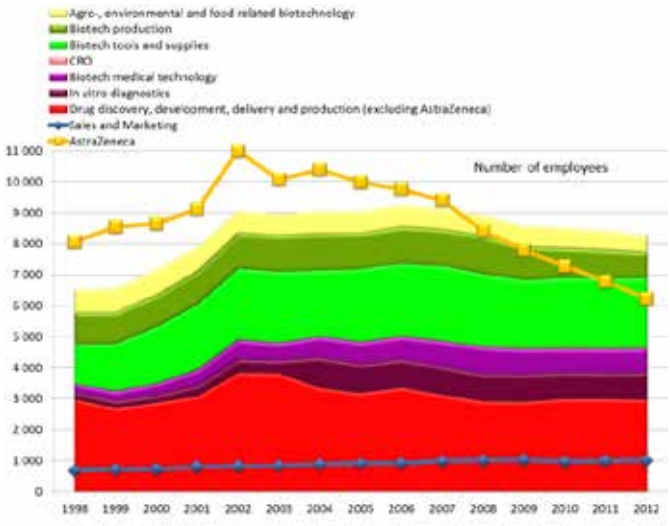
The overlap between the pharmaceutical and biotechnology sector is significant. Especially due to the number of companies in the drugs segment, including AstraZeneca, being categorised as belonging to both sectors. The biotechnology sector includes more than 15 513 employees in almost 400 companies with the majority of employees active in 'drug discovery, development, delivery and production'. AstraZeneca is included in the biotechnology sector since a large activity is drug discovery using biotechnology. This is also the case for many other companies in the drugs business segment leading to a significant overlap between the pharmaceutical and biotechnology sectors. The second largest business segment is 'biotech tools and supplies'. The number of employees in sales and marketing has been nearly constant the last five years at around 1000 employees.

[23] Sandström A. "Svensk Life Science industri efter AstraZenecas nedskärningar" VA 2012:07 (2012)

Table 7 The size of the biotechnology industry in Sweden 2012

BUSINESS SEGMENT	NO. EMPLOYEES	NO. COMPANIES
DRUG DISCOVERY, DEVELOPMENT, DELIVERY AND PRODUCTION (EXCLUDING ASTRAZENECA)	2 966	101
ASTRAZENECA	6 232	1
IN VITRO DIAGNOSTICS	870	29
BIOTECH MEDICAL TECHNOLOGY	781	30
CRO	32	9
BIOTECH TOOLS AND SUPPLIES	2 256	74
BIOTECH PRODUCTION	822	27
AGRO-, ENVIRONMENTAL AND FOOD RELATED BIOTECHNOLOGY	542	34
SALES AND MARKETING	1 012	91
TOTAL	**15 513**	**396**

Figure 28 The size of the biotechnology sector in terms of employees, years 1998-2012

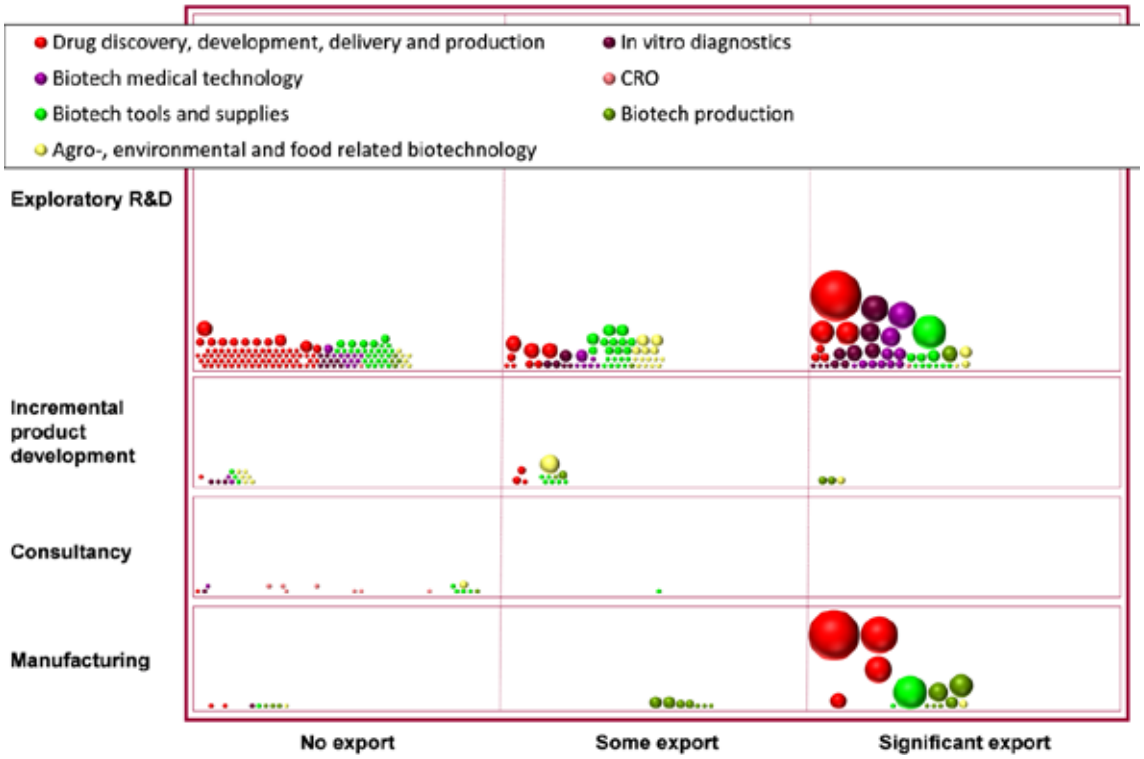


Since most of the drug discovery and development companies are also categorised under the biotechnology sector and due to the dominant size of that segment, the decline in recent years is apparent also in the biotechnology sector. The 'biotech tools and supplies' business segment has always been a significant contributor to the number of employees in the biotechnology sector in Sweden and the employment in the segment has been fairly constant since 2003, at around 2 200-2 300 employees.

The peak year for the entire biotechnology sector was also 2002. Since then, the number of employees has declined by almost 5 400, of which almost 90 percent, or 4 780 employees, depends on AstraZeneca. This sector too, includes a large number of small academic spin-off companies with exploratory research, especially in drug discovery and biotech tools and supplies.

In the latest five-year period, outside drug companies, the changes in number of employees have been little. The most significant change is the decrease in number of employees in biotech production (minus 400 employees).

Figure 29 Bubble diagram showing medical technology companies active in R&D, consultancy or manufacturing in Sweden in 2012 [bubble size (volume) is proportional to the number of employees]



The proportion of biotechnology companies which are categorised as belonging to the "Exploratory research" activity is even larger than for pharmaceuticals, 75 percent. Only 10 percent of the companies are categorised to "Incremental product development" and 6 percent are categorised as consultancy companies. Since most of the contract manufacturing companies in the pharmaceutical sector are not involved in biopharmaceutical manufacturing they are not included in the biotechnology sector, thus the number of manufacturing companies are few. The biotechnology sector is overestimated in the sense that the AstraZeneca manufacturing unit in Södertälje is not biotech production. This is due to that companies are not split according to different internal business segments.

Of the companies with R&D, consultancy and/or manufacturing 21 percent have significant exports and 27 percent have some export. Again, the consultancies and the smallest companies have no export. Since those companies are an extremely large proportion of the total population, as much as 66 percent of the companies have no export. At the same time they only represent 816 employees (less than 6 percent). The companies with significant exports however, represent 85 percent of the employees in the biotechnology sector. It is not possible to identify the total biotech exports in public statistics.

5 The business segments – global trends and Swedish dynamics

In this chapter, the development of the business segments comprising the Swedish life science industry is described as well as some insights into global trends. Only companies with their core competence and major part of their business devoted to life sciences are included. Life science companies focusing on sales and marketing are not included in the analysis in this chapter. The chapter begins with a brief description of international trends regarding life science policies.

International trends regarding Life Science policy

The links between preclinical research and benefits reaching patients is often identified as being too weak and strengthening the ties is in focus in several countries. It is often referred to as translational medical research, or going ”from bench to bedside”. This unfortunately gives an image of a linear process in only one direction instead of an iterative collaborative exchange between research and clinical practice as well as industry and other parts of the innovation system. New initiatives, re-organisations, new types of collaborative efforts and investments are being launched to support both the innovation processes in life sciences and achieving a more effective and innovative healthcare system.

In 2012, the Swedish Agency for Growth Policy Analysis performed a study on international life science policy on commission of the Ministry for Education and Research[24]. The analysis addressed issues such as the transfer of knowledge and results from research to products, therapies and applications; the conditions for clinical research and clinical trials; and strategic investments in research as well as in research infrastructure. Studied countries included USA, Canada, Switzerland, the Netherlands, United Kingdom, India and Japan. Some results from the study are summarised below.

The emphasis on life sciences in the studied countries is motivated by economic growth, knowledge production, disease treatment and health promotion. At the same time, indicators suggest that investments in the sector made during later years have not fully resulted in the expected effects. The increasing complexity and associated costs in life science research as well as the conditions for clinical research is high on the agenda. These discussions has led to a reform pressure on the systems level as well as in new and innovative methods for research and innovation, translational initiatives, new ways for collaborations as well as regulatory reforms. Some of the identified trends are listed below:

- Ambition to build life science ecosystems where basic research, corporate research and innovation, clinical research, healthcare, education and market efforts are integrated. Systems efforts appear to be most common in the United Kingdom.

[24] Björling S., Lindberg M., Karlsson A, Hashimoto S., Muranyi-Scheutz A and Wikström M., ”Vad händer inom Life Sciences internationellt? Nuläge och trender i utvalda länder” Tillväxtanalys (2012)

- Initiatives for, and investments in strategic research areas and/or research infrastructure are present in all the studied countries. There is a clear ambition to ensure that the responsibility for specific research/innovation areas do not fall between the areas covered by individual government agencies.
- Translational initiatives to strengthen the transfer of knowledge generated by research activities, to clinical applications, therapies and products are abundant. Translational efforts often include collaborative or cooperative efforts between actors through funding programs, new research centers or networks.
- The number of clinical trials has been reduced in many of the studied countries during the last decade and the conditions for clinical research as well as its connections to preclinical research are often deemed to be suboptimal. New mechanisms have been developed to improve the conditions for clinical research through funding programs, clinical research centers, infrastructure initiatives and regulative reforms.
- Some of the new initiatives and mechanisms for collaborations have components of open innovation, freely available data and shared resources.

All in all a number of similar reforms and changes relating to life sciences are underway in the studied countries. These relate to issues including steering and management as well institutional and organisational forms.

Thus areas in focus have included translational networks in particular disease areas and increased collaboration at agency level. Other initiatives have included public private partnerships in chosen strategic areas: incentives for collaboration between academia, industry and the healthcare system, launching new centres of excellence, cluster initiatives, seed financing to start-up companies etc. Initiatives are launched both in countries with a long tradition of life science innovation such as the USA, United Kingdom and Denmark and countries with rapidly growing scientific excellence and commercial activities in life science like South Korea and Singapore.[25]

An example of recent life science strategies launched is the one in the UK, presented in 2011[26]. It included a number of initiatives on the government agency level. For instance initiatives to make MHRA, Medicines and Healthcare products Regulatory Agency, more efficient leading to faster approval of innovative pharmaceuticals, but also initiatives to promote patient access to innovative treatments. Other activities aim at promoting the development and use of innovative manufacturing technologies.

A GBP 300m UK Research Partnership Investment Fund, managed by the Higher Education Funding Council for England, will provide investment in higher education research facilities and strategic research partnerships. Nine project of between GBP 32-150m each was launched in 2012, which will support collaboration between academia, charities and industry[27].

[25] http://www.vinnova.se/life_science_benchmarking
[26] https://www.gov.uk/government/publications/uk-life-sciences-strategy
[27] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/36684/12-1346-strategy-for-uk-life-sciences-one-year-on.pdf

Prime Minister David Cameron in 2012:

> "The life science industry is truly a jewel in the crown of our economy. There are around 380 pharmaceutical companies based in the UK, employing nearly 70 000 people, with an annual turnover of £30bn. In addition, the medical technology and medical biotechnology sectors together employ over 96 000 people with a combined annual turnover of around £20bn."

The investments also included GBP 130m to stratified medicine and a GBP 180m fund for life science commercialisation. Web-based solutions concerning information on clinical trials have been launched, also with an ambition to make citizens more prone to participate as well as initiatives to collect and use clinical data. Biomedical research centers in Cambridge, Oxford and London are being formed and are intended to collaborate to improve clinical research. Educational efforts in collaboration with industry have been initiated and new funding for R&D in SMEs has been made available.

The Patent Box initiative has been launched to continue to attract investments from for example Big Pharma. It means a reduced corporate tax on profits related to British patents or IPR. The budget for 2013 meant a reduced tax by 10 percent which can be compared with the ordinary corporate tax being 23 percent. GlaxoSmithKline, the largest pharmaceutical company in the UK, in 2012 announced that the Patent Box affected their decision to invest GBP 500m in one new and one expansion of manufacturing units in the UK.

Apart from the healthcare related applications of life sciences, also sustainable development, for instance targeting increased and more effective use of renewable raw materials has received increased attention internationally. Biotechnological applications in the environmental area have for instance the potential to continue to lead to more effective manufacturing processes, end of pipe and recycling solutions. This also regards sensors for environmental and security monitoring of for example production processes, distribution chains and for outdoor conditions.

In the latest Swedish government research bill in 2012 a number of initiatives targeting life sciences were launched. Initiatives described in the bill entail an increase in the resources allocated to all areas of research and innovation of SEK four billion by 2016. Along with the increase in the previous research and innovation bill, this means an increase of around SEK nine billion over eight years. Other investments in the bill will to some extent also benefit life sciences but the ones listed in the table below specifically targets life science.

Table 8 Specific life science initiatives in the government research and innovation bill in 2012[28]

MEASURE	MSEK 2013	MSEK 2014	MSEK 2015	MSEK 2016
SCIENCE FOR LIFE LABORATORY	150	150	150	200
RESEARCH ON INFECTION AND ANTIBIOTICS [VR]	40	75	75	75
RESEARCH ON AGEING AND HEALTH[FORTE AND VR]	50	100	100	100
PHARMACEUTICAL DEVELOPMENT [KTH]	40	40	40	50
INSTITUTE FOR SUSTAINABLE PROCESS DEVELOPMENT AND CATALYSIS [SP]	100	40	10	-
NATIONAL SUPPORT FOR COORDINATION OF CLINICAL STUDIES	30	40	40	50
CLINICAL TREATMENT RESEARCH [VR]	20	50	75	75

** VR- the Swedish Research Council, Forte- the Swedish Research Council for Health Working Life and Welfare, SP-Technical Research Institute of Sweden, KTH-Royal Institute of Technology*

The process development and catalysis activities of SP are housed in the previous R&D facility of AstraZeneca in Södertälje. So is the new initiative Swedish Toxicology Research Center, which is a collaboration between eleven Swedish universities starting its operations in 2014. As has already been mentioned, a number of life science operations such as companies, regional authorities, university departments etc. have already moved into the old facilities of AstraZeneca in Lund now called Medicon Village.

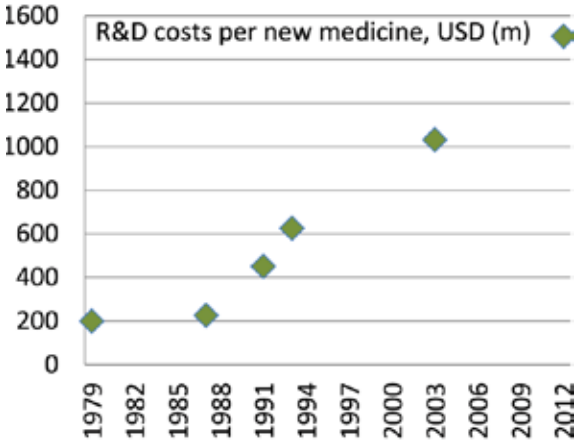
5.1 Drug discovery, development, delivery and production

R&D costs

All new medicines introduced on the market are the result of lengthy, costly and risky research and development. By the time a medicinal product reaches the market, an average of 12-13 years will have elapsed since the first synthesis of the new active substance[29]. The cost of researching and developing a new chemical or biological entity was estimated at USD 1 506m in 2012[30]. The corresponding cost in 1979 was USD 100m or according to another source USD 199m[31], i.e. regardless of which source is correct the increase has been steep. Of the present costs about 40–75 percent is estimated to be related to clinical trials[32].

[28] http://www.regeringen.se/sb/d/108/a/207030
[29] The Pharmaceutical Industry in figures - Edition 2013, EFPIA
[30] Mestre-Ferrandiz et al, Office of Health Economics, December 2012 (http://ohematerials.org/NMECost/index.html#/0)
[31] Hansen R. "The pharmaceutical development process: Estinates of the development costs and time and effects of the proposed regulatory changes." In Chien R.A. ed. Issues in pharmaceutical economics, Lexington, M.A., D.C. Heath and Company, p 151-191 (1979)
[32] Pore M., Pu Y. Pernenkil L., Cooney C.L. "Offshoring in the Pharmaceutical Industry. In: The Offshoring of Engineering: Facts, Unknowns, and Potential Implications." http://www.nap.edu/catalog.php?record_id=12067 (2008)

Figure 30 Estimated full cost of bringing a new chemical or biological entity to market[33]



World-wide market development

There is a rapid market growth for emerging economies such as Brazil, China and India. In 2012 the Brazilian and Chinese markets grew by 16 percent and 21 percent respectively, compared to an average market growth of minus two percent for the five major European markets and minus one percent for the US market[34]. In 2012, North America accounted for 41 percent of world pharmaceutical sales compared with 27 percent for Europe. Concerning sales of new medicines, launched during the period 2007-2011, 62 percent of the sales were on the US market, compared with 18 percent on the European market.

Figure 31 Global sales of pharmaceuticals and estimates for the years 2011-2014

Source: IMS Health

Global spending on medicines annually will grow to nearly USD 1 200bn by 2016, as the emerging markets, biologics and generics contribute a greater proportion of spending. By 2016,

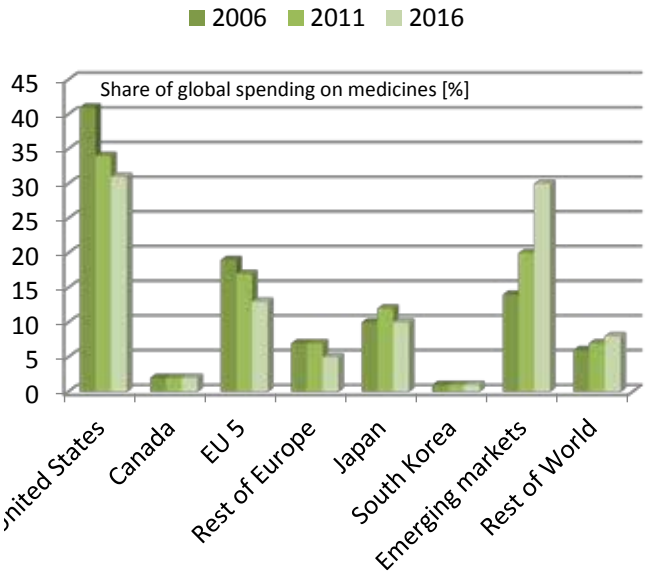
[33] J. Mestre-Ferrandiz, J. Sussex and A. Towse, "The R&D cost of a new medicine, Office of Health Economics", (Hansen, 1979; Wiggins, 1987; DiMasi et al, 1991; OTA, 1993; DiMasi et al, 2003; Mestre-Ferrandiz et al, 2012) (2012)

[34] IMS Retail Drug Monitor – February 2013 IMS Health

developed markets are expected to decline to 57 percent of global spending due to for example patent expiries, increased cost containment actions by payers and the sustained impact of the global economic crisis felt in these countries since 2008. At the same time the emerging markets[35] share of spending is expected to increase by 10 percentage points to 30 percent of global spending over the next five years. The emerging countries will thus double their spending on pharmaceuticals over the next five years to USD 35-45bn in 2016. In Europe, growth is expected to be in the -1 percent to 2 percent range through 2016, compared to 3.8 percent 2007-2011.[36] Classes with the highest levels of spending on medicines in general in 2016 are expected to include cancer, diabetes and asthma/chronic obstructive pulmonary disease.

An accelerated shift to the use of generic medicines is expected, both from an unprecedented level of patent expires in the US, and from volume-driven growth in the largely generic-using emerging markets. At the same time, lower-cost versions of expensive biologic medicines, biosimilars, will continue to be launched, though slowly, and will account for only USD 4-6 billion, or 2 percent, of the USD 200-210bn in spending on biologics by 2016. Fewer biosimilar products than expected have been approved thus far.

Figure 32 Proportion of global spending on medicines by geography



Source: IMS Health

In Sweden, the sales of medicines was reduced by SEK 600m in 2012 (SEK 36 100m in total) compared to 2011. This means that the sales are almost back on the level of 2010. This is the first time a reduction has occurred as long as Apotekens Service has kept track of the sales, that is year 2000. It is primarily the prescription drugs which have declined.

[35] China, Brazil, India, Russia, Mexico, Turkey, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan and Vietnam
[36] The Global Use of Medicines: Outlook Through 2016 Report by the IMS Institute for Healthcare Informatics (2013)

At the same time as the Big Pharma companies have consolidated, the number of companies on the pharmaceutical market has increased, partly due to the Big Pharma companies outsourcing more of the innovation processes. Thus they gain flexibility and do not have to maintain staff for these services. According to McKinsey the number of companies who are claiming a piece of the revenues from pharmaceutical sales has doubled[37]. As in many other industries, the big integrated global companies are more and more becoming companies assembling the relevant knowledge and orchestrating the innovation process, often moving their in-house capabilities to the later stages of the innovation process and increasing the focus on market access and sales.

Challenges in pharmaceutical development

The pharmaceutical industry is facing a number of challenges. These for example include:

- Patent expiries and generics gaining ground
- Cost containment actions by payers and delays in market access
- Reduced R&D productivity, that is increasing R&D costs per new medicine[38]
- Radical innovation – radical risk
- Steep regulatory demands
- Week pipeline – unmet medical needs often demand radical innovations
- Prerequisites for industry-healthcare system collaboration

In 2011, generics accounted up to 75 percent of the total for prescription drugs, which can be compared with 56 percent in 2005[39]. Of the top 20 best-selling pharmaceuticals in 2010, eight came off patent by the end of 2012, representing more than USD 25bn in sales. Thus sales of Seroquel (AstraZeneca), zyprexa (Eli Lilly), plavix (Sanofi) and lipitor (Pfizer) have all fallen in sales since they have gone off their patent protection. The anti-cholesterol drug Lipitor has been one of the best-selling drugs worldwide for a number of years and has been a major source of income for the world's biggest drug company Pfizer. Lipitor therapy can cost up to 168 USD per month. Lipitor was first marketed in 1998, and by 2006 it had reached peak sales of USD 12.9bn, accounting for 27 percent of the company's revenue. In 2010, Lipitor still accounted for nearly 16 percent of total revenue. Seroquel's worldwide sales amounted to USD 5.3bn in 2010, or nearly 16 percent of AstraZeneca's revenues. Plavix was the second best-selling drug in the world, with USD 9.4bn in global sales in 2010. This drug has been marketed jointly by Sanofi-Aventis and Bristol-Myers Squibb, and the cost of therapy averages about 162 USD per month. In 2010, BMS recorded USD 6.7bn in Plavix sales, or 34 percent of its total revenues. Sanofi recorded sales of nearly USD 3bn, or 7 percent of its 2010 revenues. The pharmaceutical industry anticipates a loss in sales of more than USD 80bn in the next few years due to patents expiring and generic substitution. Generics cost 30-80 percent less than the original medicines.

At the same time many markets are facing ageing populations with more patients being multi-sick. Many indications lack satisfactory treatments both for large populations and rare diseases.

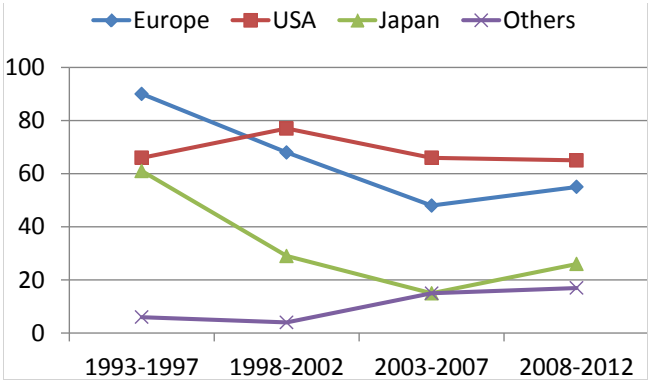
[37] McKinsey Quarterly "A wake-up call for Big Pharma" (2011)
[38] Pammolli F., Magazzini L. och Riccaboni M. "The productivity crisis in pharmaceutical R&D" Nature Reviews, Drug discovery, Vol. 10 (2011)
[39] Kandybin A.och Genova V. "Big Pharma's Uncertain Future" Booz & Company in New York (2012)

The technical risk is difficult to estimate in radically innovative pharmaceutical development where effective treatments are missing or unsatisfactory. It is likely to always be associated with a high technical and financial risk – at the same time as there are great opportunities. There are many areas in medicine lacking effective treatments; for example diabetes, Alzheimers and Parkinsons disease, effective pain relief and most serious forms of cancer. It has also become more and more clear that regarding radical innovation, the risk is not significantly reduced as the projects moves to later phases of development. Many projects even fall in Phase III, after huge investments.

Both private and public payers discourage incremental innovation and investments in follow-on drugs in already established therapeutic classes, mostly by the use of reference pricing schemes and bids designed to maximize the intensity of price competition among different molecules. In established markets, innovative patented drugs are sometimes reimbursed at similar levels as older drugs. As a consequence, R&D investments tend to focus on new therapeutic targets, which are characterized by high uncertainty and difficulty, but lower expected post-launch competition.[40]

New drugs on the way to be approved include treatments of osteoporosis, respiratory disease, thrombosis, multiple sclerosis and cancer. The figure below shows the number of new approved drugs.

Figure 33 Number of approved drugs, new chemical or biological entities (NME and BLA), according to nationality of parent company



Source: SCR IP – EFPIA calculations

The largest R&D investments in Big Pharma companies are today being made in cancer followed by cardiovascular and metabolic diseases, neuroscience, pain and infectious diseases. To an increasing extent more medicines are today being developed which compete with, and has to be significantly better than established treatments.[41]

[40] Pammolli F., Magazzini L. och Riccaboni M. ”The productivity crisis in pharmaceutical R&D” Nature Reviews, Drug discovery, Vol 10, p 429-438 (2011)
[41] Pammolli F., Magazzini L. och Riccaboni M. ”The productivity crisis in pharmaceutical R&D” Nature Reviews, Drug discovery, Vol 10, p 429-438 (2011)

Big Pharma and Big Biotech companies have increased their R&D-investments by 147 percent between 1993 and 2004 whereas the number of applications for FDA approval only increased by 38 percent during the same period[42]. Since the mid‑1990s, pharmaceutical R&D productivity has experienced a downturn. From 1998 to 2008, the number of NMEs approved per year declined (although it has been roughly constant since 2005), whereas development times and R&D expenditures have all increased. One reason for increasing R&D costs is that an increasing proportion of the projects fall in all phases of clinical development. The increase is especially seen in phase II and III. Among the reasons for the failures is that the pharmaceutical industry focus on more difficult research areas and targets. The options regarding possible research areas are increasing due to the identification of new possible targets. A focus on previously non-validated targets increases the risk. Particularly the US companies are focusing on such high risk and large potential market areas. At the same time there seems to be little difference in profitability between US and European companies.[43]

Previous ways to meet the challenges

A way for Big Pharma to add to the pipeline has been mergers and acquisitions. The mergers and acquisitions involving Big Pharma companies have led to fewer and larger Big Pharma companies which are now downsizing. Some of the mergers occur after a long standing collaboration between the involved companies, like for instance the acquisition of Schering Plough by Merck & Co whereas Pfizer and Wyeth were strangers before the Pfizer takeover. Schering had a pipeline with about 18 biopharmaceuticals in phase III in 2009 and a geographically wide-spread sales organisation and Wyeth had a strong portfolio of products and a promising pipeline, especially in biopharmaceuticals, for example in the CNS area. In both those deals, executives described potential costs savings as a big benefit whereas improving the coordination on product development was the reason given when Roche, which already had owned a majority of Genentech since 1990, acquired the company completely. The mergers have also been motivated by gaining access to complementing competences, e.g. the AstraZeneca acquisition of biopharmaceutical competence through the acquisition of MedImmune.

The companies have also focused on fewer indications within fewer disease areas and primarily targeted those with large potential markets. Improving established drugs has been seen as a way to extend patent rights, e.g. to suit larger patient populations. Changes in working methods have primarily come about due to technological breakthroughs like the use of High Throughput Screening technology and later on biotechnology (recombinant DNA-technology, genomics and proteomics). Collaboration with academia has continued and also the collaboration with both intermediary and integrated biotechnology companies. The down-sizing the last decade has been dramatic. Pfizer reduced its number of employees by 49 000 between 2005 and 2010 (Pfizer had about 110 000 employees in total in 2011) and AstraZeneca has reduced its number of employees by more than 30 000 since 2007.

[42] Jones A. & Clifford L. Nat. Rev. Drug Discov. 4, 807–808 (2005)
[43] Pammolli F., Magazzini L. och Riccaboni M. ”The productivity crisis in pharmaceutical R&D” Nature Reviews, Drug discovery, Vol 10, p 429-438 (2011)

Present changes and initiatives to reduce the risks

Big Pharma companies continue to downsize their in-house R&D capabilities and are now looking for new working methods, ways to collaborate and ways to reduce the risks. The trends are however dividing when it comes to focusing on core competencies[44], prescription drugs, or spreading the risks by diversifying into areas such as; generics, biosimilars, diagnostics, veterinary medicine, over the counter drugs, nutraceuticals, regenerative medicine etc. [45] There are examples of both strategic choices among the Big Pharma companies. Some also start smaller R&D units intended to be more flexible, sometimes originating from acquired small biotech firms. All firms are on the other hand moving away from thinking that a large share of their future innovations will stem from in-house R&D, being the source of ideas, owning all rights and run everything from early discovery to marketing and sales. Now they see many different potential sources of ideas and are ready to share the work in all development phases, even with competing Big Pharma companies. More of the R&D processes is also outsourced, generating new opportunities to niched companies as suppliers of products and services in areas such as identifying and validating targets, drug delivery solutions, toxicology and safety studies, pharmacology etc. A common focus is also biopharmaceuticals.

There are a number of ways which both Big Pharma companies and smaller dug discovery companies try to reduce the risks.

- Orphan drugs – aiming for a rare medical condition means less regulatory demands making it easier to gain marketing approval to incentivise companies to perform R&D regarding diseases affecting small patient populations
- Reformulation, follow-on drugs – extending the use of an active substance by continuing developing the formulation of the drug to possibly reach new patient populations, e.g. leading to more effective, simplified or improved dosage
- "Re-indication" – using approved active substances for a completely new indication meaning that the substance does not have to go through all of the approval procedures again, e.g. regarding possible side effects
- Big Pharma - Big Pharma partnering – sharing risks either to gain pre-commercial synergies or commercial projects aiming to share profits possibly by dividing geographical markets between them
- Downsizing in-house R&D – scouting for external projects from academia, or more often small biotech companies means cutting costs and gaining flexibility (partnering, mergers and acquisitions)
- Open platforms[46] – often collaboration involving public funding, academic and SME partners (possibly also several Big Pharma companies[47]) and often concerning big data,

[44] Pfizer divesting its operations concerning nutraceuticals and veterinary medicine
[45] Examlpes include Abbott Laboratories splitting into two companies; prescription drugs and diagnostics; J&J in OTC, diagnostics and prescription drugs; Novartis in generics prescription drugs, Roches efforts in diagnostics, also claimed to have synergies with drug discovery R&D in target identification and screening of substances.
[46] Chesbrough, H.W "Open Innovation: The New Imperative for Creating And Profiting from Technology" Harvard Business School Press, Boston (2003) and Chesbrough, H.W. "Open Business Models: How to Thrive in the New Innovation Landscape" Harvard Business School Press, Boston (2006)
[47] E.g. 'Innovative Medicines Imitative' involving partnering between the European commission and the pharmaceutical industry

substance libraries[48][49], clinical data and such things[50] [51] or primarily academic initiatives in disease areas such as malaria or tuberculosis [52]

- Personalised/stratified medicine using companion diagnostics – either using genetic testing or biomarkers before or after starting the treatment meaning that side effects or lack of response to treatment that could jeopardize the possibility of approval or market access, can be avoided
- Combinatory medicine – combining established medicines leading to an improved treatment with reduced technical risks since the individual drugs have already been approved[53]

An extensive study[54] identified the inventors of all 252 new drugs approved by the US Food and Drug Administration (FDA) from 1998 to 2007 and their places of work, and also classified these drugs according to innovativeness. The study investigated the contribution of different types of organisations and regions to drug innovation during this period. According to the study, intermediary biotech companies or academia contributed to about half of the radically innovative drugs as well as to half of the drugs addressing unmet medical needs. These organisations however contributed to a smaller proportion of the total number of new medicines.

An example of changed working methods is the description of the new way of performing R&D in neuroscience by AstraZeneca. AstraZeneca's virtual Neuroscience Innovative Medicines Unit with only about 40 employees is intended to orchestrate the reduced neuroscience portfolio through a complex network of partners, e.g. several niched companies. With a number of unmet medical needs in the neuroscience area, AstraZeneca thus intends to keep a foothold in this field, even if it is largely a virtual presence.

The future innovation processes for developing innovative medicines is thus uncertain. At the same time as this restructuring is taking place the Big Pharma companies are still showing profits and some are also showing increasing sales. The downsizing of in-house operations will make resources available for investments and collaborations. Thus many countries are launching activities to become increasingly attractive for Big Pharma R&D investments.

Clinical trials

Prerequisites for commercial clinical trials and clinical research in general are often high on the agenda when the innovation climate for development of health innovations is discussed in Sweden. The most common clinical trials evaluate new drugs, medical devices, biologics,

[48] NIH gaining access to more than 20 substanses from AstraZeneca, Pfizer and Lilly which they discontinued to develop
[49] Weigelt, J. “The case for open-access chemical biology” EMBO Rep. 10, 941–945 (2009).
[50] https://innovation.gsk.com/IAG-OpenInnovationTeam.aspx
[51] Barnes, M.R. et al. ”Lowering industry firewalls” Nat. Rev. Drug Discov. 8, 701–708 (2009); Louise-May, S., Bunin, B. & Ekins, S. “Towards integrated Web-based tools in drug discovery” Touch Briefings Drug Discov. 6, 17–21 (2009)
[52] www.mmv.org; http://www.osdd.net/; http://www.collabrx.com/; www.healthcommons.net; sagebase.org; http://www.andi-africa.org
[53] For example the Glaxo Smith Kline and Pfizer collaboration in the field of combinatory medicine for HIV treatment in the formation of the company Viiv Healthcare
[54] Kneller, R. “The importance of new companies for drug discovery: origins of a decade of new drugs” Nature Reviews, Vol. 9 (2010)

psychological therapies, or other interventions. Clinical trials are required before a national regulatory authority approves marketing of the innovation. The number of commercial clinical trials is decreasing in Sweden, as in many other countries in Western Europe and North America. Reasons often mentioned are increased competition from for example Eastern Europe and Asia and that the conditions for clinical trials are perceived to have deteriorated. In for instance China it is also required that some trials are performed on the population in China to access the Chinese market after approval. Among the positive effects of clinical trials being performed in a country mentioned are that the collaboration between academia, industry and the healthcare system generate a mutual knowledge exchange which benefits both patients and the innovation climate. Patients benefit from an increased awareness in the healthcare system of, and interest in, the most innovative treatments.

There is a slight shift in the localisation of clinical trials from USA and EU to Asia pacific and the Americas outside USA. Sweden has the most clinical trials in the Nordic countries but as for the other Nordic countries, the number of trials is declining.[55] The decision on where to locate clinical trials is dependent on such things as quality, cost efficiency, reliability (e.g. regarding estimates of the time it will take), productivity and sometimes also access to future markets. Important issues are also established networks to the healthcare system and access to good CROs. It is according to Big Pharma representatives often the case that the schedule does not hold and that there are problems getting the assured patient populations.

According to a study[56] by the Swedish Agency for Growth Policy Analysis the trend of a decreasing number of clinical trials in several western European countries and an increasing number in Eastern Europe and Asia is credible, but has perhaps slowed between 2008 and 2012. This is possibly a result of increased costs in Eastern Europe and measures to improve conditions, for example in Great Britain. The trend in Sweden, however, seems to be slightly more negative than in Belgium, Denmark and Great Britain.

As a consequence of the decreasing clinical trials, several countries are changing their system for clinical studies. The studies are seen as important, not only for financial reasons but also since they are a crucial part of the ability to translate biomedical research and can contribute to a positive development within the field of health care, for example speed up introduction of new forms of treatment and access to new pharmaceuticals. The measures initiated can in most cases be grouped into the following areas:

- Collaborations on research and innovation between funding providers, care organisations, universities, charitable organisations and companies as well as measures to improve the research and innovation culture in the care system.
- Recruitment of and access to patients, for example through clinical research networks, information portals and the build-up of accessible patient cohorts.
- Greater transparency, for example through broad dissemination of information about trials as well as simplified and accelerated procedures for issuing licences, ethical reviews and access to resources in the care system.

[55] www.clinicaltrials.gov
[56] Ledin A., Wikström M and Zeilon P. Clinical trials - Policy initiatives and trends Svar Direkt 2014:01 (2014)

- Information initiatives, including innovative ways of using information from the care system as well as international marketing.
- Improved cost-effectiveness and quality awareness.

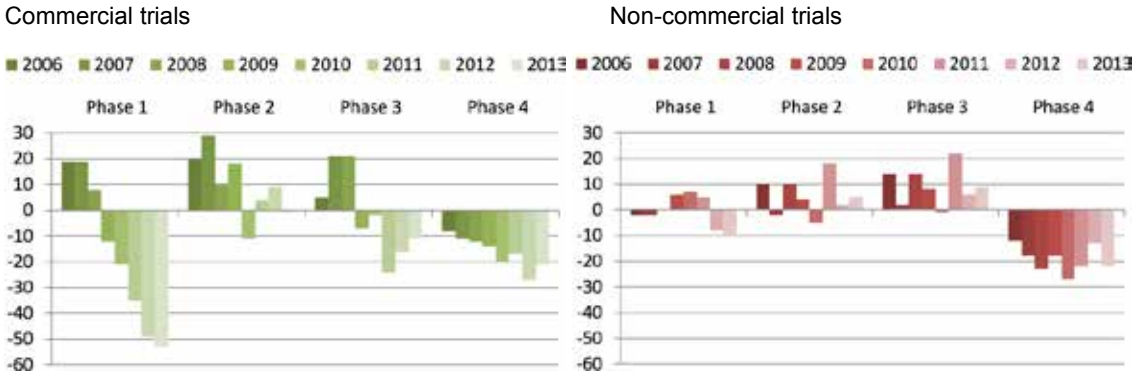
The interviews performed as part of the study, pointed to the importance of cost-effectiveness, quality, punctuality, good opportunities for collaboration and access to well-characterised patients as central factors in decisions on location. Denmark and Great Britain seem to have come a relatively long way in their measures to attract trials, which British experts consider are already having positive effects. In Belgium, which has a long tradition of clinical trials, such measures are largely still at the planning stage, but the discussion is similar to the ones in Denmark and Great Britain. The USA still dominates clinical studies, although the number of trials in phases I to IV has fallen in recent years (2008–2012), albeit from a very high level, and the USA will undoubtedly continue in the lead for the foreseeable future. The main thrust of the American measures is to stimulate translation and change the regulatory prerequisites for pharmaceutical development, including trials. Interviews in Canada indicate that Great Britain's reforms in the field of life sciences are considered an interesting model. In Canada the plan is now to increase initiatives aimed at translation and improve the prerequisites for clinical studies. In China, the number of clinical studies is increasing rapidly, but from a low level.

Several of the countries studied, and others, are working pro-actively to improve the conditions for clinical studies, which Sweden needs to consider. Regardless of what measures Sweden adopts in the short term, an iterative process is probably also needed to develop the long-term conditions for types of trials where Sweden can be particularly competitive. These might for example include trials on well-characterised patient populations, studies where international collaboration with competitive research and innovation milieus are of importance and studies where Sweden's advantages in informatics and registers contribute added value. At the same time, the general regulatory framework for trials, according to the study, probably needs to be strengthened in several areas. A deeper collaboration on clinical trials between the Nordic countries might be desirable in the long term, for example regarding identifiable patient populations and recruitment of test subjects.[57]

As mentioned earlier, the number of commercial clinical trials in Sweden has decreased each year since 2007 (Figure 34). This has affected all phases and the total decrease was 38 percent 2007-2013. Phases I and IV have declined the most, with minus 71 and 70 percent respectively. At the same time, Phases II and III have declined with little over 20 percent each. The trend is not the same for non-commercial trials where the largest total number of trials was performed in 2011. Of the clinical trials in 2013, 75 percent were commercial and 25 percent non-commercial, a similar distribution as for previous years. For the commercial trials, most trials were in Phase III, almost twice as many as in phase II, six times as many as in Phase I and almost ten times the number of Phase IV trials. The total numbers of clinical trials in Sweden in 2013 were 336 and the number of trials has ranged between 319 and 336 the last four years. Between 2006 and 2009 however, between 414 and 440 clinical trials were performed each year.

[57] Ledin A., Wikström M and Zeilon P. Clinical trials - Policy initiatives and trends Svar Direkt 2014:01 (2014)

Figure 34 The number of commercial (green) and non-commercial (red) clinical trials each year 2006-2013, relative to the reference year 2005



Source: The Medical Products Agency Sweden (EudraCT database)

Phase III requires large patient populations which means that several clinical trials nodes usually need to collaborate. With a small population like Sweden's this means that there is often need of international networks to perform larger trials. As has already been mentioned, the R&D cost of a new chemical or biological entity was in 2012 estimated at USD 1 506m[58] and the process can take 10-15 years. Of that cost, 40–75 percent is related to the recruitment of patients[59] [60].

Sweden is in interviews referred to[61] as having the positive prerequisites of a well-functioning medical product agency, good CROs and well qualified local employees in Big Pharma companies which together leads to trials of good quality. The fact that the prerequisites for follow-up studies later-on also are good speaks for Sweden as a location for clinical trials. Swedish studies are also known for keeping to the schedule and the goals regarding quality. The results are also helped by the fact that personnel involved have good ICT-skills. According to the industry, issues to be improved include a more uniform way to handle formalities and better prerequisites for healthcare personnel to participate. Healthcare personnel bring forward that it is difficult to get the time necessary to take part and that there are no incentives to participate, i.e. that clinical research or participating in clinical trial processes is not incentivised by the employer. It is sometimes stated that Sweden is a particularly good location for phase IV trials due to the way patients are monitored etc., despite this a clearly negative trend is seen in the statistics in Figure 34.

Traditional drug licensing approaches are based on binary decisions. At the moment of licensing, an experimental therapy is presumptively transformed into a fully vetted, safe, efficacious therapy. A discussion has started about possible other ways to proceed to yield safe,

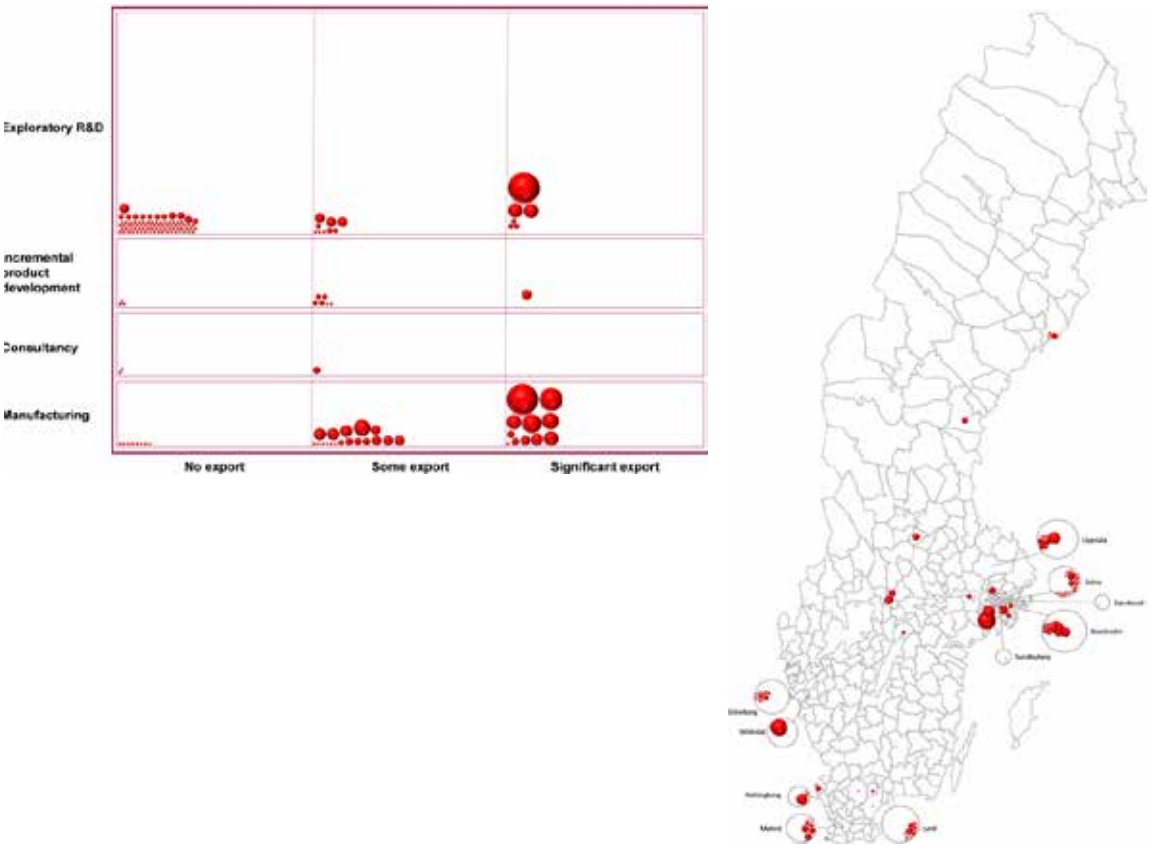
[58] Mestre-Ferrandiz et al, Office of Health Economics, December 2012 (http://ohematerials.org/NMECost/index.html#/0)
[59] Pore M, Pu Y. Pernenkil L, Cooney CL (2008) "Offshoring in the Pharmaceutical Industry. In: The Offshoring of Engineering: Facts, Unknowns, and Potential Implications." http://www.nap.edu/catalog.php?record_id=12067 (2008)
[60] Lustgarten "A Drug testing goes offshore" Fortune, August 8, 57-61 (2005)
[61] http://www.vinnova.se/upload/EPiStorePDF/va_12_07.pdf

but quicker and less costly ways to approve new drugs for instance by adaptive licensing. Adaptive licensing approaches are based on stepwise learning under conditions of acknowledged uncertainty, with iterative phases of data gathering and regulatory evaluation.[62]

Swedish trends and dynamics

The drug discovery, development, delivery and production business segment in Sweden comprised almost 12 400 employees in almost 150 companies in 2012, not including sales and marketing companies.

Figure 35 Companies in 'drug discovery, development, delivery and production' in Sweden in 2012, shown in the bubble diagram as well as geographically distributed according to the location of company facilities



This business segment is by far the largest in the life science industry, with 42 percent of the employees in 2012. AstraZeneca constitutes more than half of the business segment in terms of number of employees. Also, Swedish Orphan Biovitrum (393 employees) contribute a significant number of employees involved in drug discovery and development, followed by BioInvent and Active Biotech (both with 76 employees), Medivir (53 employees) and KaroBio (51 employees). Pfizer Health has been categorized as biotech production. Companies starting with a core competence in drug delivery are today also often drug development companies and

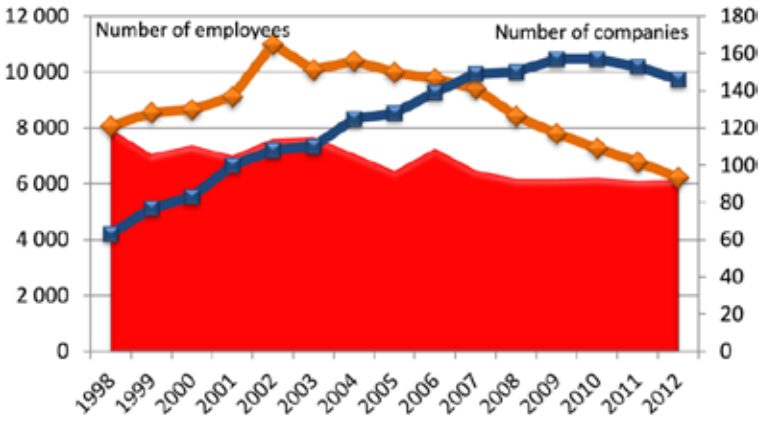
[62]H-G Eichler et.al. Clinical Pharmacology & Therapeutics (2012); 91 3, 426–437. doi:10.1038/clpt.2011.345

this is for example the case for Orexo (more than 90 employees), Oasmia Pharmaceutical (more than 70 employees) and Camurus with almost 30 employees. All in all, 12 companies in drug development have been identified as using active substances already used in other drugs and focusing on re-formulation and re-indication.

In drug production, the dominant players are Fresenius Kabi (clinical nutrition, more than 1000 employees), McNeil (divested from Pfizer in 2006, now part of Johnson & Johnson and producing Nicorette, almost 700 employees) and the Recipharm group, also with about 700 employees in total. Swiss Octapharma (blood plasma replacement and also biopharmaceuticals, almost 700 employees) is placed in this business segment but could equally well have been placed in the biotech production business segment due to the activities in biopharmaceutical production. It was kept in this business segment due to it being divested in 2002 from Pharmacia Corp, categorised to this segment. Other large manufacturing companies are Cambrex Karlskoga (almost 300 employees) and Apoteket Produktion & Laboratorier (almost 500 employees). Kemwell (headquartered in India) and Ccs Healthcare have almost 200 employees each.

Companies developing new drugs are predominately found in the activity category "Exploratory research" (vertical axis in Figure 35). In 2012, there were 93 such companies. The majority of the small start-up companies, with little or no export and low turnover, are found in the Stockholm and Malmö/Lund regions. Many of the employees in the segment are found in the manufacturing activity category, largely due to the above mentioned large manufacturing units, the AstraZeneca unit in Södertälje being the largest with almost 3 000 employees.

Figure 36 Number of employees of the company AstraZeneca (orange line) and the rest of the business segment (red surface). Also shown is the number of companies (blue line) years 1998-2012



As has already been mentioned the number of companies in this business segment has increased steeply. Even though the number has decreased since the peak year in 2008, still it has increased by 130 percent since 1998. In 2012 146 companies were categorized to the drugs business segment. As is seen in Figure 36 the development of the number of employees outside AstraZeneca has been almost completely flat since 2008, with about 6 200 employees.

In a study by SwedenBIO the drug development pipeline in Sweden was analysed[63]. About 50 percent of the companies involved in exploratory research have ongoing clinical trials and of these companies, most are micro-sized (79 percent). The pipeline contains nearly 70 products being developed in Sweden and in clinical development, excluding all AstraZeneca projects. The projects are distributed across many therapeutic areas, where the development of new cancer drugs shows the by far greatest number of both preclinical and clinical projects. Most of the companies involved in those Cancer trials are found in Stockholm/Uppsala and Lund. Cancer is followed by Infection, CNS, Gastrointestinal and Diabetic/Metabolic diseases. Of the 67 unique molecules identified in the study, 31 were large molecules, including antibodies, therapeutic vaccines, cell therapies, hormones and peptides.

Of the 81 ongoing clinical trials identified, most projects are in Phase II, 47 projects, compared to 19 in Phase I and 14 in Phase III. Since the study has been performed annually since 2006 it is also possible to analyse the development over time. Seven of the projects reported last year progressed to next phase this year. One Phase III project reported the previous year was filed for registration. The number of trials in Phase II has never been as many as in 2013.

Since the year 2000 Swedish companies have received orphan drug designations from EMA and/or FDA for nearly 50 drugs. During 2012 the following Swedish companies got orphan drug designations: Albireo, Axcentua Pharmaceuticals, Cortendo and Premacure. According to the respondents of the drug development pipeline survey 2013, 20 percent of the projects in Phase I-III are projects intending to apply for orphan drug designation or has already received it (response rate 74 percent). The market for orphan drugs is relatively small due to the low number of patients. However, according Thomson Reuters, the total market value was estimated to be USD 50bn at the end of 2011[64]. An incentive with developing orphan drugs is also that the reduced time to market attracts investors and the orphan proportion in the Big Pharma pipelines also seems to be increasing.

The development of the orphan drug Plenadren by the company DuoCort Pharma[65] is a successful example of a relatively quick and cheap development process, one reason being that it was an orphan drug with a less costly trials period as a result. Also, the active substance was already established and therefore well known, also reducing the need for clinical trials. Plenadren is a modified-release hydrocortisone tablet given once daily to patients with primary adrenal insufficiency. The project is one example, among many, of a development process being performed in a network of partners and consultants and lead by a company having very few in-house staff. Other examples include the companies Premacure and Albireo. Premacure was developing a drug for treatment of an eye indication, ROP (retinopathy of prematurity), a rare and potentially blinding eye disorder that primarily affects premature infants. The project was in a Phase II trial before the company was acquired based on the clinical results and potential future market. Both DuoCort and Premacure were acquired for large up-front payments and future conditional payments, by foreign companies, Viropharma and Shire respectively. For

[63] The Swedish Drug Development Pipeline 2013, by SwedenBIO with support from VINNOVA and Business Sweden (2013)
[64] The Economic Power of Orphan Drugs, 2012, Thomson Reuters
[65] www.pulsinvest.se

Plenadren, ViroPharma payed an upfront closing cost of SEK 220m. Additionally, there are contingent milestone payments of up to SEK 860m associated with manufacturing, sales thresholds and territory expansion. Swedish Recipharm was in 2012 contracted by ViroPharma to complete commercial scale-up manufacture of Plenadren. Shire has now acquired also Viropharma. Albireo took a project for a treatment of chronic constipation, spun-out from AstraZeneca through to Phase III trials, with few in-house staff and a relevant external network. The project is now licensed to Ferring Pharmaceuticals and Ajinomoto Pharmaceuticals.

Since there may be subgroups in the intended patient population not answering to the treatment or who show negative side-effects from the treatment, the use of biomarkers to identify which patients should receive the treatment is increasing. This makes it possible, or increases the chances to get a drug approved. This is sometimes called companion diagnostics and leads to personalised or stratified medicine. The decision on treatment may be built on genetic tests, biomarkers before administrating the drug to the patient or biomarkers after administrating the drug to the patient to monitor patient response (e.g. metabolites). Reducing patient populations however also means reducing the revenues unless the price per patient is increased. Regulatory agencies including the FDA and the EMEA are now actively encouraging the use of companion diagnostics in the development and use of prescription drugs. In the SwedenBIO survey, almost 20 respondents claimed that they are developing companion diagnostics in at least one of their projects.

5.2 In vitro diagnostics

Mergers, acquisitions and the divesting of business units are frequent on the global scene also in the in vitro diagnostics area. Part of this is related to changed strategies of Big Pharma companies since they to some extent have included diagnostics business units. The degree of centralisation when it comes to laboratory services related to diagnostics varies between countries dependent on how the health care system is organised. This may mean that products need to be modified depending on the market. The trend with companion diagnostics is thus far to a large extent developed in parallel with the drug development process and by the same organisations. A companion diagnostic device can be an in vitro diagnostic device or an imaging tool that provides information that is essential for the safe and effective use of a corresponding therapeutic product[66]. In the future this could also become a business area for specialised niche companies with competences in diagnostics.

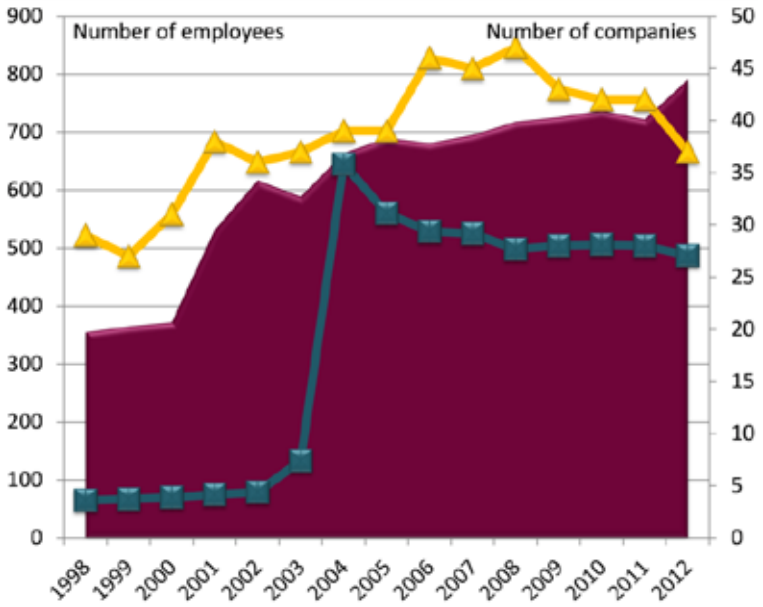
The by far largest company in in vitro diagnostics is US Thermo Fisher Scientific owned Phadia (acquisition in 2011, allergy diagnostics and diagnostics of autoimmune diseases), with 420 employees. Phadia was divested from Pfizer (Pharmacia origin) in 2004 explaining the sharp increase in employment that year. The second largest company is US HemoCue (blood analyses of glucose and haemoglobin levels), with more than 300 employees, followed by US Cepheid (previously Sangtec Molecular Diagnostics) with almost 130 employees. There are three more companies in the segment with more than 50 employees: Boule Medical, Euro-Diagnostica and

[66] FDA

Allergon (a subsidiary of Phadia) and yet another seven companies with ten or more employees in 2012.

The total number of employees in the business segment was in 2012 almost 1 300 in 37 companies. The business segment has had almost the same size since 2004. Companies which have grown include Hemocue and Cepheid. Six micro-sized companies have however stopped employing and only one company has entered the business segment 2012 compared to 2011, leading to a net decrease in the number of companies by five.

Figure 37 Number of employees of the company Phadia (blue line) and the rest of the 'in vitro diagnostics' business segment (burgundy surface). Also shown is the number of companies (orange line) years 1998-2012



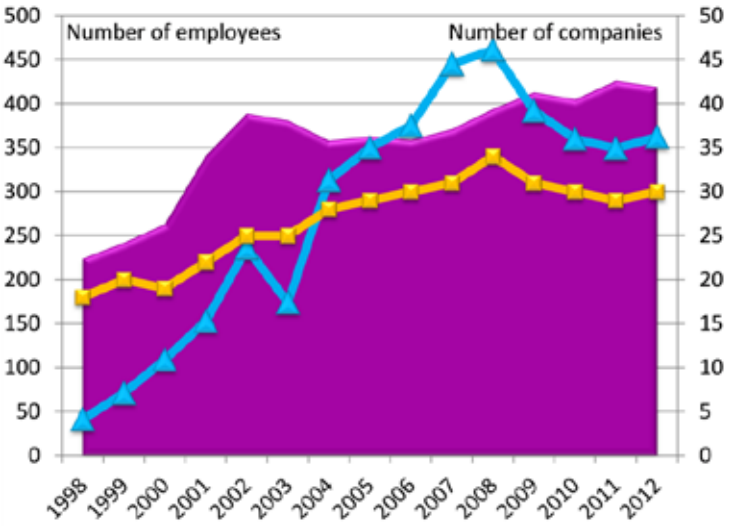
Phadia is located in Uppsala with the subsidiary Allergon in Skåne. Most of the other diagnostics companies are found in Stockholm/Uppsala followed by Skåne and Gothenburg (Figure 5).

5.3 Biotech medical technology

The biotech medical technology business segment includes the large company Q-Med (hyaluronic acid, since 2011 owned by Swiss Galderma) as well as Vitrolife (IVF-technology), with more than 360 and 130 employees respectively. Both these companies have grown from companies with less than 50 employees during the studied time period. Then follows a group of companies with about 30 employees each: Dipylon Medical (previously CMA Microdialysis, now owned by US Harvard Apparatus), Bohus Biotech, Biora (owned by Straumann), Carmeda (owned by W L Gore & Aassociates) and Olerup Ssp. There used to be a number of micro-sized companies developing regenerative medicine solutions which have stopped employing. A number of the micro-sized companies remaining are in the area of biodegradable biomaterials.

In total the business segment consists of 805 employees in 31 companies including 19 micro-sized companies. The number of companies has increased from18 to 31 1998-2012. The number of employees peaked in 2008 and has since then declined with about 50 employees.

Figure 38 Number of employees of the company Q-Med (blue line) and the rest of the 'biotech medical technology' business segment (purple surface). Also shown is the number of companies (orange line) years 1998-2012



5.4 CRO

Contract research organisations (CRO) provide support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis. It may provide such services as biopharmaceutical development, biologic assay development, commercialisation, preclinical research, clinical research, clinical trials management, and pharmacovigilance. CROs that specialise in clinical-trials services can offer their clients the expertise of moving a new drug or device from its conception to FDA/EMA marketing approval.

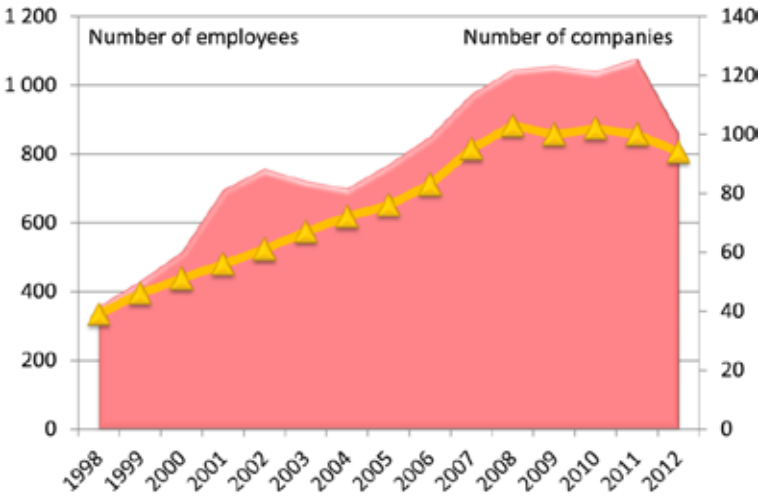
As was seen in Chapter 4, most of the identified CROs are focused on pharmaceutical development. It should be noted that most companies supplying for example services concerning preclinical biotechnological research are in the present study found in the biotech tools and supplies business segment. Thus almost all companies categorised to this segment, work with issues related to the regulatory processes of pharmaceutical, biotechnology, and medical device products.

The largest CRO in Sweden is Quintiles (about 150 employees), followed by Trial Form Support and PPD Scandinavia with about 100 employees each. In total there are about 25 companies with more than five employees in the segment. The reduction in clinical trials in Sweden has affected the CROs negatively and a few have gone out of business in recent years. Quintiles has reduced its number of employees by more than 130 employees since 2011, primarily due to a decision to reduce activities relating to phase I clinical trials in Sweden. The company is thus responsible for much of the downturn in 2012 seen in Figure 39. Most CROs

are found in the Stockholm/Uppsala region followed by Lund and a few companies are also found in Gothenburg.

In total the business segment includes about 860 employees in 94 companies. The segment has increased by about 500 employees 1998-2012 despite a decrease by almost 200 in the latest three-year period.

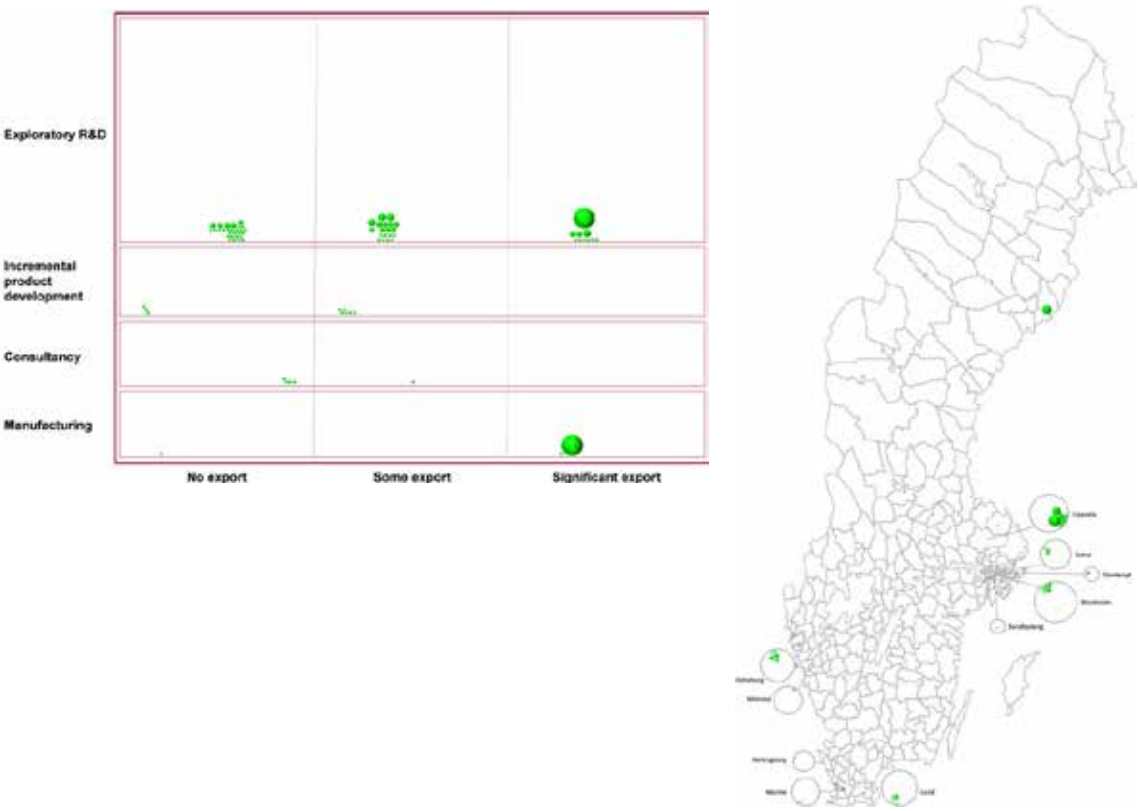
Figure 39 Number of employees of the CRO business segment (pink surface) and the number of companies (orange line) years 1998-2012



5.5 Biotech tools and supplies

The increased outsourcing by large corporations is apparent in many industries. It has in the Swedish life science industry led to an increased number of specialised companies supplying products and services used in the innovation processes or in manufacturing. Many of those are found in the biotech tools and supplies business segment. The products are primarily used in preclinical research in companies and academia, i.e. aimed at making the development of new medicines more effective through the use of new technology. Products and services are also developed for use in industries outside the ones developing healthcare related products, such as chemicals, food, agricultural and environmental applications.

Figure 40 Companies in the 'biotech tools and supplies' business segment in Sweden in 2012, shown in the bubble diagram as well as geographically distributed according to the location of company facilities



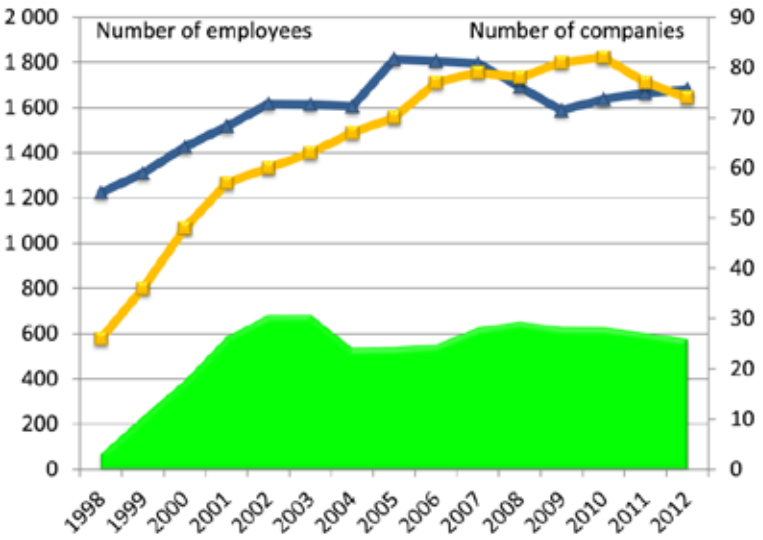
The business segment employs over 2 250 in 74 companies and is greatly dominated by US GE Healthcare Bio-Sciences (e.g. bioseparation) with almost 1 700 employees (see Figure 41) and an origin in Pharmacia. The company has R&D in Uppsala and manufacturing in Uppsala and Umeå (Figure 42). The company has grown in Sweden during the studied period and in 2009 a new manufacturing unit for chromatography media was inaugurated in Uppsala. In 2006, GE Healthcare Biosciences acquired Biacore (biomolecular interaction), a spin-off company from Pharmacia in 1984.

Other companies include Biotage (microwave synthesis), Gyros (miniaturised and automated immunoassays), Halo Genomics (recently acquired by Agilent Technologies, Netherlands), French Cellectics (stem cells, previously Cellartis) and Affibody (tools for protein analysis) all with between 30 and 60 employees. There are many small academic spin-off companies with exploratory R&D with little or no export.

An example of a growing academic spin-off company is Olink, which started employing in 2004 and has grown to 28 employees in 2012. Olink's molecular technologies analyse cell signalling pathways by microscopic visualisation and also quantifies endogenous protein interactions and modifications. The technology is commercialised through licensing to industry partners such as Affymetrix, Life Technologies, and through the spin-out companies Qlinea and

Halo Genomics (now part of Agilent). There is a clustering of companies in Uppsala. The number of companies peaked in 2010 and has since then declined by six.

Figure 41 Number of employees of the company GE Healthcare Biosciences (blue line) and the rest of the 'biotech tools and supplies' business segment (green surface). Also shown is the number of companies (orange line) years 1998-2012



The total number of employees was more than 2 250 in 2012 and has since 1998 grown by more than 960 employees. The employment has been almost the same in the latest three-year period.

5.6 Biotech production

This business segment includes companies focusing on biomolecules, cells or microorganisms for use in healthcare-related products such as diagnostics and pharmaceuticals. It also includes biotechnological production of chemicals used by the chemical, forest, pulp and paper industries and other products such as ingredients used by the food industry. Much of the development of biotechnological processes outside healthcare-related products, occur in large companies that do not have biotechnology as their core activity. Thus those companies are not included in the business segment. The ones being included in those fields are a few intermediary companies, commercialising academic research.

In total the biotech production segment included 27 companies with 822 employees in 2012. It has in total decreased by almost 180 since 1998. After a few years of growth in the beginning of the period the segment started to decline in 2008 and in the latest three-year period the employment has been reduced by 240. The decline in recent years is largely due to DSM Antiinfectives closing its site in Strängnäs in 2009.

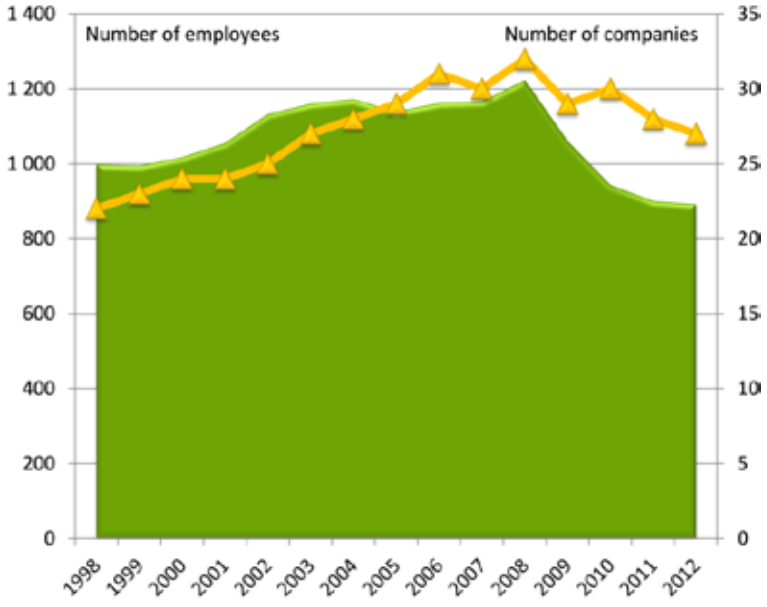
In 2011, US Repligen Corporation acquired Novozymes Biopharma Sweden, focusing on the manufacture and supply of growth factors used in mammalian cell culture and Protein A affinity ligands used in the production of monoclonal antibodies. Repligen Sweden with 70 employees in Lund was thus formed in 2012. This newly established company was unfortunately not included in the database when the present dataset was compiled and is thus not included in the

statistics for the whole life science industry. It has however been added in the graph below (Figure 42) showing the dynamics for this business segment.

Concerning healthcare-related products the largest companies identified are Pfizer Health (275 employees), Polypeptide Laboratories (165 employees) and Crucell Sweden (111 employees). At Pfizer Health in Strängnäs, Genotropin, a growth hormone is manufactured, but also Fragin, a low-molecular-weight heparin as well as anti-thrombotic agents. Crucell manufactures vaccines but it is also a contract manufacturer (CMO). Polypeptide Laboratories manufactures proprietary and generic GMP and non-GMP peptides.

Internationally there is an increased focus on enhancing the use of renewable materials and more effective and environmentally sound production processes. Biotechnological production methods are often resource effective and based on renewable raw materials. For Sweden, special interests are new high value added products based on forestry raw materials. Large companies with industrial biotechnology as part of their competence but not as their core activity (and thus not included in the present study) for instance include the specialty chemical company Perstorp and the economic association Södra (processed forest products). The pulp and paper industry has R&D activities within modern biotechnology, mostly in collaboration with university groups and industrial research institutes. The biotechnological companies with activities related to this area and included in the present analysis are for instance: Xylophane (barrier material for packaging based on natural carbohydrates), Invekta Green, Protista International, Organoclick and Appeartex AB, all micro-sized companies but Xylophane which had 12 employees in 2012.

Figure 42 Number of employees of the company employees in the 'biotech production' business segment (green surface) and the number of companies (orange line) years 1998-2012



5.7 Agro, food and environmental biotechnology

Companies engaged in plant improvement, functional food and environmental technology also use modern biotechnology. The applications for instance concern the treatment of water used in processes, wood protection against fungi or the use of naturally occurring micro-organisms with desired characteristics concerning function and toxicity.

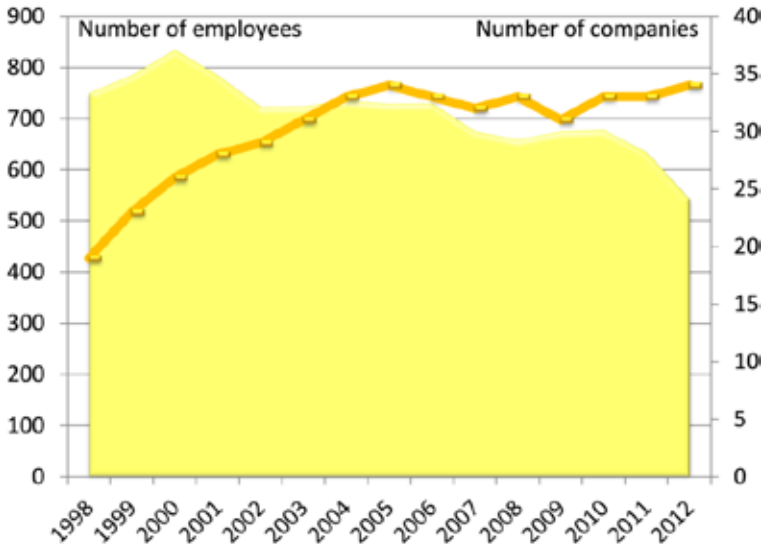
The companies in agrobiotechnology include Syngenta Seeds with about 180 employees whereas Lantmännen Sw Seed (previously Svalöf Weibull), have reduced their number of employees drastically in recent years and now only employs 34. It may be that some of the activities today are integrated in another part of the Lantmännen group. There is also a small forest biotechnology start-up, SweTree Technologies with about 20 employees.

In food related biotechnology we have Biogaia (probiotics), Kemikalia (the enzymes chymosin and bovine pepsin), Swedish Oat Fiber, Astareal (micro algal production and natural astaxanthin) and Probi (probiotics), all with about 20 employees.

Companies in environmental biotechnology include for instance Anoxkaldnes (water treatment) and Ekologisk Technologi (soil treatment).

In total the business segment employs 542 personnel in 34 companies in 2012, a reduction of more than 200 employees since 1998. Most of the decline occurred in the latest three-year period.

Figure 43 Number of employees of the 'agro, food and environmental biotechnology' business segment (yellow surface) and the number of companies (orange line) years 1998-2012



5.8 Implantable devices – active and non-active

Since 2007, Swiss Nobel Biocare and Swiss Straumann have been the dominate players in the worldwide dental implant market with very similar sales figures in recent years. In 2007, Nobel Biocare almost hit the USD 1bn sales mark, USD 966m to be exact. Since then the Nobel

Biocare's sales have declined. Conversely, Straumann's sales have continued to increase, albeit at a relatively slow rate. Their sales together represented approximately 57 percent of the worldwide implant market in 2010[67]. The other three firms that have consistently ranked in the top five firms are: Dentsply International, Biomet 3i, and Zimmer Dental. The three companies in 2010 were responsible for 14 percent of the global sales. Thus the Dentslpy inclusion of the Astra Tech operations affirms the company as number three in terms of global sales. In 2010, 31 companies obtained FDA marketing clearance to sell dental implants in the United States in addition to the top-five companies. Both Straumann and Nobel Biocare obtain the majority of their sales outside of the US. However, Nobel Biocare is more dependent on North American sales than Straumann. The major firms are offering digital solutions for implant placement using their brands.

The number of competitors is thus proliferating and the new firms are likely to compete on price unless they offer clinically significant advantages and not only offer acceptable clinical solutions. The dentistry business is price sensitive and may gravitate to lower-cost substitute implants.

Apart from Nobel Biocare and Dentsply with together 1 371 employees in Sweden, other companies with operations related to dental implants include firms such as Promimic (implant surface to accelerate osseointegration), Tigran Technologies (porous titanium granules and a debridement product) and Ostell (instruments that measure the stability of dental implants), all with around 10 employees.

Other companies developing bone anchored applications based on the principle of osseointegration include companies such as Cochlear Bone Anchored Solutions with almost 200 employees (bone anchored hearing aids) and Integrum with 12 employees (bone anchored prosthesises).

Other implantable devices include the pacemaker. However, St. Jude Medical in 2011 decided to close the R&D and manufacturing operations related to the pacemaker in Sweden and move the manufacturing to Malaysia. The pace maker is a Swedish invention from the 1950-ies and the operations included more than 600 employees before the decision. St. Jude Medical also has operations in Sweden in the areas of cardiac mapping and visualisation systems, catheter-based ablation devices and vascular closure devices which will not be affected by the decision and are part of the business segment electromechanical medical devices.

The business segment also includes companies such as Atos Medical (ear, nose, throat implants) and Elos Medtech Timmersdala (surgical and orthopedics implants and instruments), with 153 and 136 employees respectively in 2012. Among the small-sized firms, companies such as Bone Support, Doxa, Swemac, Oticon Medical, Occlutech International and Surgical Inventions are found, all with between 10 and 20 employees.

In total the business segment included 36 companies with employees in 2012 and the total number of employees was almost 2 500. The segment has grown by almost 1400 employees

[67] Dental implant market update, Anaheim group 2011

since 1998 and the development has been almost flat the latest three-year period, despite the decline of St Jude Medical.

In Figure 44 the development of employees for Nobel Biocare, Dentsply, St Jude Medical and the rest of the business segment are seen, as well as the number of companies. For Dentsply, also the activities outside dental implants such as catheters and surgical instruments are included in the statistics.

AstraTech (now Dentsply) has seen a sharp increase in number of employees and in 2012 included about 970 employees (red line in Figure 44). Since the pacemaker part of St Jude Medical is ceasing its operations in Sweden, the blue line will continue its decline. The invention on which Nobel Biocare was founded dates back to 1965 and was further developed in close collaboration with specialist dental care providers of the county councils in Sweden. In 1983 the Procera method of high-precision, repeatable manufacturing of dental crowns was developed in Gothenburg. Nobel Biocare in 2013 also announced its intension to cease R&D activities in Sweden and instead focus R&D efforts to the facilities in Switzerland, USA and Canada. This does not affect a major part of the employees in Nobel Biocare, but is an important issue considering that Gothenburg has been a stronghold for R&D activities and innovations in the osseointegration research area. At the same time Australian Cochlear (previously Entific) has shown a strong growth in Gothenburg during the entire studied period.

Figure 44 Number of employees of the following companies: Dentsply (red line), the pacemaker part of St Jude Medical (blue line) and Nobel Biocare (green line); the rest of the 'implantable devices – active and non-active' business segment (light blue surface). Also shown is the number of companies (orange line) years 1998-2012

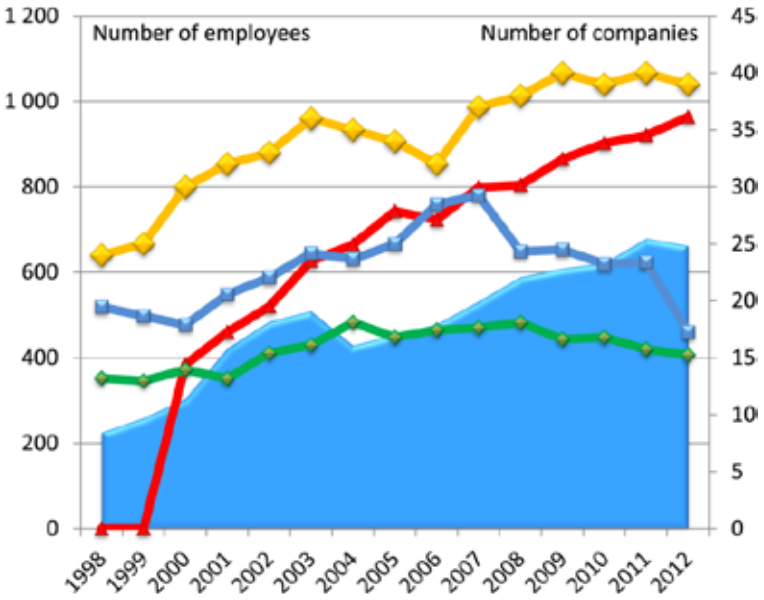
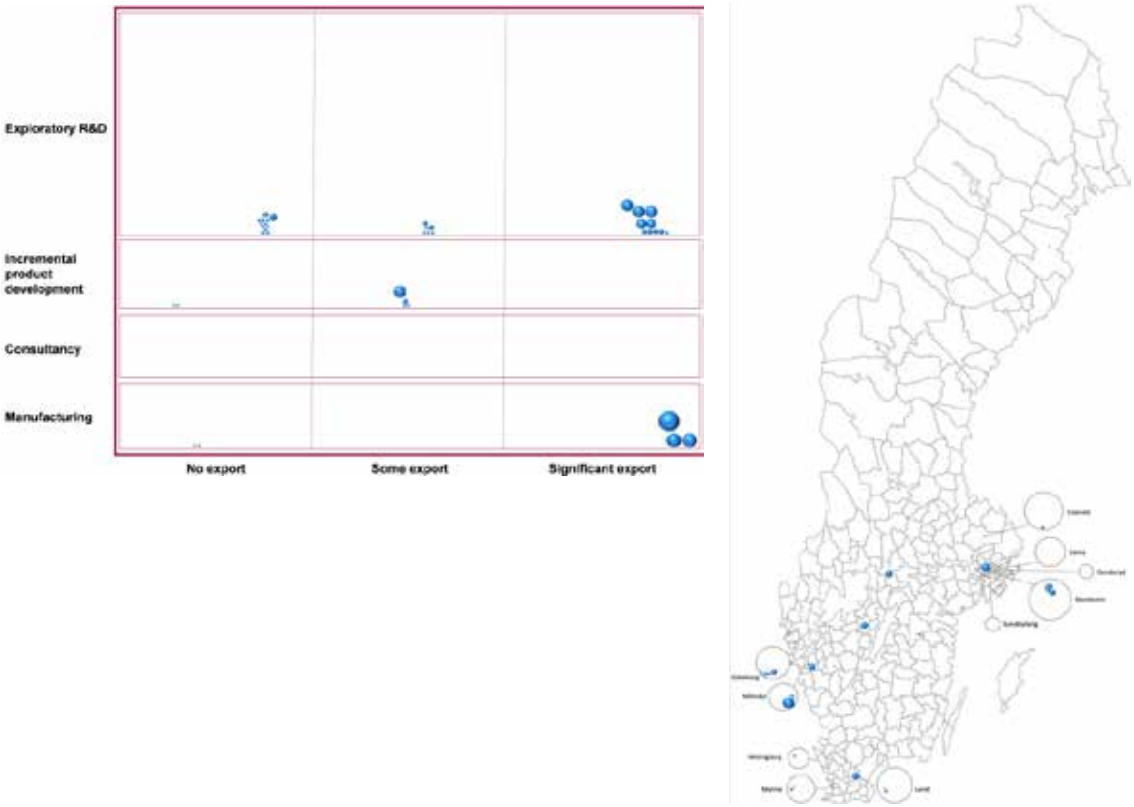


Figure 45 Companies in the 'implantable devices – active and non-active' business segment in Sweden in 2012, shown in the bubble diagram as well as geographically distributed according to the location of company facilities



Nobel Biocare has units in Stockholm, Gothenburg and Örebro, St Jude has had its activities in Stockholm, whereas Dentsply and Cochlear have all operations concentrated to Gothenburg and Atos Medical is located in Skåne. There are also some manufacturing units which are co-located with R&D, for which all employees are visualised in the R&D bubble when the unit is smaller than 500 employees. Some small- and micro-sized companies do not have any exports whereas all large firms have significant export.

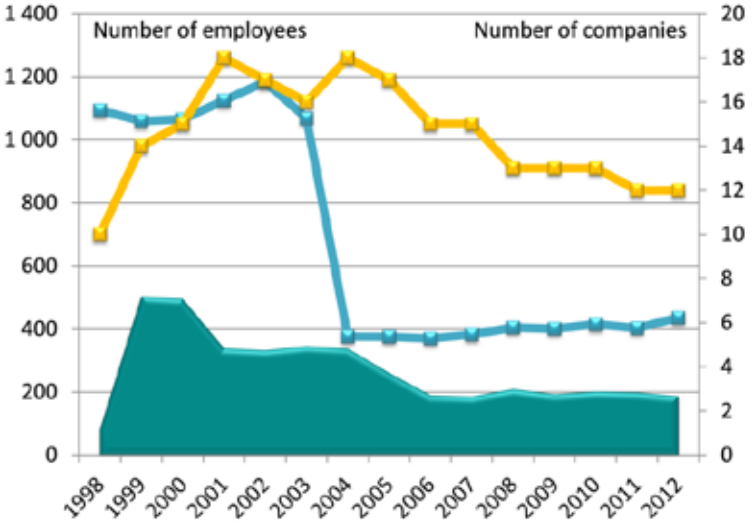
5.9 Anaesthetic and respiratory devices

The largest company in Anaesthetic/respiratory devices is by far Maquet Critical Care in Stockholm. The company develops life support systems stemming from a Swedish invention from the 1950-ies, had 440 employees in 2012 and is part of the Getinge group. It was in 2003 that Getinge acquired the life support systems part of Siemens Elema. At the same time, the X-ray part of the company was closed in Sweden and the operations moved within Siemens, to Spain and Germany. Since the figures for years previous to the acquisition by Getinge reflect the dynamics of Siemens Elema, this is the reason for the sharp dip in employees in 2004 for Maquet Critical Care.

The number of companies in the field is 12, a decrease by six companies since the peak years 2001 and 2004. Other companies in the group are US Breas Medical AB (e.g. home care

ventilation), Masimo Sweden (ultra-small gas monitoring probes which can be integrated into patient monitors, anesthesia delivery systems and ventilators; previously Phasein), Aerocrine (monitoring of nitric oxide) and Chinese Mindray Medical (gas analysers for anaesthesia equipment, previously Artema Medical), all with between 30 and 75 employees in Sweden in 2012. All in all, the companies in the business segment employ 620, thus the Maquet share is 70 percent of the total employment in the segment. The employment has been almost the same in the latest three-year period.

Figure 46 Number of employees of the companies Maquet Critical Care (blue line) and the rest of the 'anaesthetic and respiratory devices' business segment (blue-green surface). Also shown is the number of companies (orange line) years 1998-2012

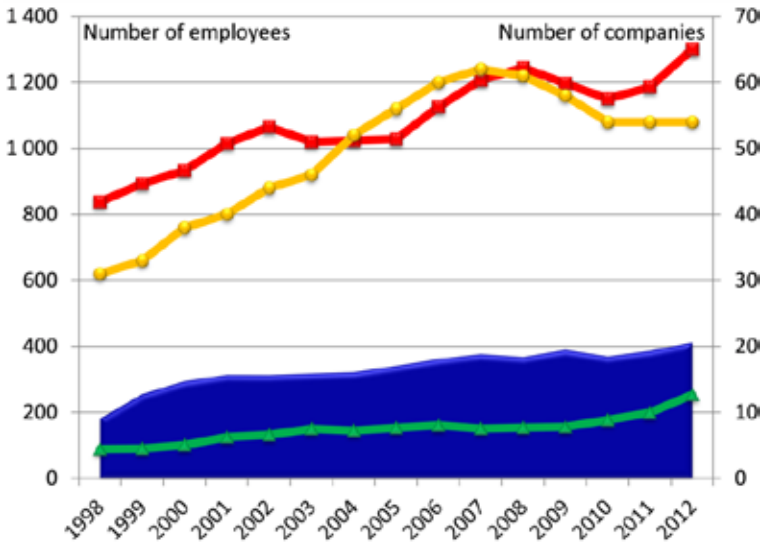


5.10 Electromechanical medical devices

The business segment electromechanical medical devices is dominated by two companies, Gambro in Lund in dialysis devices invented in Sweden in the 1940-ies, and (1000 employees) St. Jude Medical Systems in Uppsala in coronary diagnostics, interventional cardiology and haemostasis management (250 employees). There are 11 companies with 10 to 55 employees and 41 micro-sized companies in the group. The companies develop such things as devices for microscopy, microvascular diagnosis, electrotherapy, patient monitoring, chest compression etc. The segment in total includes 1712 employees in 54 companies. Gambro represents 61 percent of the employees in electromechanical medical devices. The segment has increased by almost 700 employees since 1998 and by 125 employees in the latest three-year period.

During the studied time period, Gambro has grown by 300 employees, St. Jude Medical Systems by 165 and the rest of the electromechanical devices business segment by 230 employees, an increase of almost 700 employees in total. The number of companies has decreased by six companies since the peak year 2007.

Figure 47 Number of employees of the following companies: Gambro (red line) and St Jude Medical Systems (green line); the rest of the 'electromechanical medical devices' business segment (blue surface). Also shown is the number of companies (orange line) years 1998-2012



Gambro was founded in 1964 and in 2013 had 8 000 employees globally, 13 production facilities in nine countries, sales in more than 90 countries and annual sales of approximately USD 1.6bn. In 2013 Gambro was acquired by Baxter International Inc. The deal combines Baxter, the world's No. 2 maker of dialysis equipment by revenue, with Gambro, the third-largest. Fresenius Medical Care AG of Germany ranks first by revenue. Gambro is considerably smaller than Baxter, which has a market value of some USD 36bn and had sales in 2012 of USD 13.9bn. Baxter has its core portfolio and pipeline in peritoneal dialysis systems and investigational home hemodialysis whereas Gambros' focus in dialyzers, devices and dialysis solutions, monitors, and acute therapies to treat patients with serious kidney, liver and lung conditions, where the treatment is generally performed in a hospital or clinic. Fresenius is market leader in the largest market, hemodialysis, Baxter in the second largest market, peritoneal dialysis and Gambro in the third largest market, renal intensive care.

The incident rate of end-stage renal disease in emerging markets is starting to accelerate as a result of lifestyle choice, sedentary lifestyle, and diet thus leading to an increased market for devices for such treatment. There is also growth in mature markets.

There is much hope for future stem cell therapies where insulin producing cells are intended to be transplanted to patients. There are still a number of hurdles before such therapies can reach patients and thus far the technology has been studied in mice.

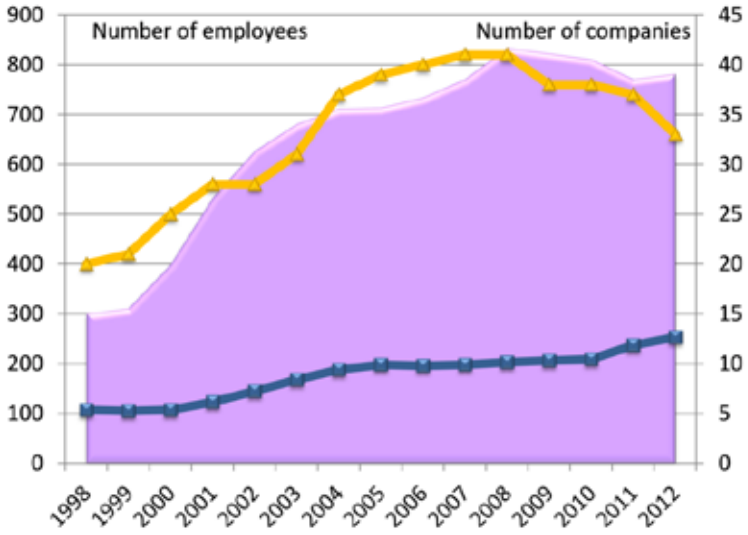
5.11 Radiation and imaging devices - diagnostic and therapeutic

The largest companies in 'radiation and imaging devices – diagnostic and therapeutic' are Elekta, developing clinical solutions for treating cancer and brain disorders using radiation therapy and radiosurgery (250 employees) and Sectra group (200 employees). Philips Digital

Mammography Sweden (previously Sectra Mamea), Gems PET Systems (cyklotrones) as well as Unfors Instruments (X-ray) each have around 100 employees. There are eight companies with 10-60 employees and 19 micro-sized companies. The companies are developing products and services in areas such as Positron Emission Tomography (PET), imaging and x-ray systems, services and equipment for diagnostic radiology and radiation therapy.

All the above mentioned companies have contributed significantly to the growth seen in Figure 48. In total, the number of employees in those six companies has grown by 530 employees. The total segment has grown by almost 600 since 1998, to a total of 1035 employees in 2012. There has been little change in the employment the latest three-year period.

Figure 48 Number of employees of the company Elekta (blue line) and the rest of the 'radiation and imaging devices - diagnostic and therapeutic' business segment (light purple surface). Also shown is the number of companies (orange line) years 1998-2012



Siemens is not included in this group since most of the Siemens operations in Sweden are focused on other branches of industry. Siemens has four focus areas of which one is Healthcare, with about 300 of the 1500 employees in Sweden. Healthcare includes both ICT solutions and medical devices such as PET, MRI and X-ray. Many of the employees in Sweden are working with medical devices, with issues such as sales, marketing, education and services related to the devices used in the Swedish health service but also with R&D issues in collaboration with clinicians at Swedish university hospitals.

Global trends include combing technologies such as for instance MR and PET, developing the visualisations further and using the devices for both diagnostics and treatment. Examples are new minimally invasive technologies in cardiology and other therapeutic areas. To develop new technologies, extensive collaboration with clinical practice is necessary throughout the innovation process. Also, integrating data from the devices with ICT tools used for electronic health records and medical informatics solutions is an increasing trend.

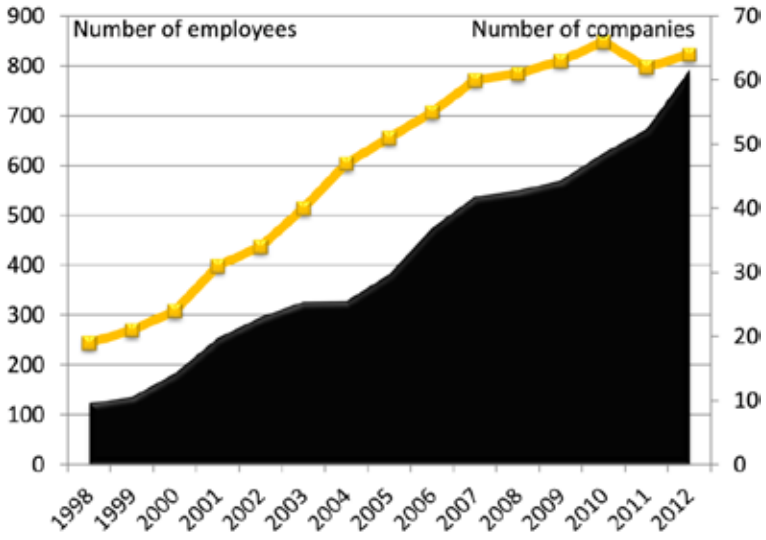
5.12 Information and communication tools (ICT)

As was described in Section 2.2 the companies can be divided in four subgroups: 1) Administrative systems, 2) Electronic health records (EHR), 3) Technical ICT as well as 4) Personal health related products for end consumers. Especially the companies in subgroup 1) and 2) have shown a steep positive development in recent years and these two groups seem to some extent also to be merging. Some of the administrative and EHR solutions are developed by large ICT corporations, with a presence in Sweden and with operations directed towards several industrial sectors and thus not included in this analysis, e.g. IBM, Evry and Siemens. For example, about 65 of the employees at Siemens Healthcare are working in the ICT area with solutions regarding the handling of medical records and add-on modules concerning patient data for the Swedish and Nordic market.

In Sweden there has been a steep growth from a low level for the business segment. Included are only companies with their majority focus in ICT solutions for healthcare applications. Compugroup Medical (patient journal systems, 155 employees) develops administrative and EHR tools. Cambio Healthcare Systems develops software to administrate and document healthcare processes (113 employees) and is beginning to merge administrative, EHR tools with medical informatics, developing add-on products based on the information collected in the administrative and EHR tools. Other examples of companies include Medhelp Care Uppsala and Diabetes tools with 47 and 8 employees each. A company in technical ICT is for instance RaySearch working with software to optimise radiation therapy (83 employees). Cogmed is a company with 11 employees developing patients training solutions for improved cognitive performance and Mentice is introducing a simulation technology based tool for surgical education (26 employees). An area with potential for growth are tools for home care, for example for monitoring patient status, including simple diagnostic tests that the patient or next of kin can administer without medical training and also including techniques for efficient communication with the healthcare system.

The business segment in total includes 64 companies with almost 800 employees of which 16 companies have ten employees or more. In Figure 49 Number of employees of the ‘information and communication tools’ business segment (black surface) and the number of companies (orange line), the development of the number of employees and companies in the ICT business segment is seen, illustrating the steep increase in number of employees from a low starting point and also that the number of companies increased until 2010.

Figure 49 Number of employees of the 'information and communication tools' business segment (black surface) and the number of companies (orange line) years 1998-2012



The possibility to monitor all patient information in an electronic health record has been discussed for a long time. The potential for more effective diagnostic support, early detection of patients at risk of developing serious conditions and better monitoring of the outcomes of alternative treatments has long been inspiring discussions, pilot initiatives and commercial development. To have a record in digital format that is capable of being shared across different health care settings; including a range of data, such as medical history, medication, allergies, laboratory test results, radiology images, vital signs, personal statistics like age and weight etc. is attractive. And demands thought through solutions taking ethical and safety issues into account.

Today it is common that suppliers of ICT solutions handling medical records develop add-on modules to handle issues like the interface between the patient and the health service (scheduling appointments, attestations etc.), reporting to national e-health services, safety and integrity solutions concerning blocking and patient consent handling etc. Large global players such as Epic and Cerner, may also enter the Swedish market, especially when there are larger procurements in the Swedish healthcare system.

Scale becomes an advantage when it comes to managing patient records, merging those tools with solutions for the interface between patients and the healthcare system and national authorities as well as adding medical informatics based solutions. Thus, also for this type of products and services, there is a trend of consolidation and moving towards oligopoly. There has already been some consolidation in the field in Sweden since the market has changed as the handling of procurement has become more centralised at the county council level.

This situation adds to the challenge for small niched companies to enter the market. The way the field will evolve will ultimately depend on the way the healthcare sector choses to work and procure in the future. The development will be affected by issues such as what level of integration of different needs in the whole health service chain that will be deemed desirable.

Also, the future organisation of the processes in the health service chain will influence the development. The procurement has become more centralised and the contracts have become more long-term. The ICT-budget in the Swedish county councils is today SEK 8.0-9.5bn per year, i.e. the same proportion of costs since 2004. The market for healthcare documentation is today dominated by six systems from five suppliers which together covers 96 percent of all users[68]. The largest suppliers and systems are:

- Siemens (Melior) – Germany
- CompuGroup (Journal 3, PMO, Take Care, Medidoc) – Germany
- Evry (Systeam Cross) – Norway
- Cambio Healthcare (Cosmic) – Sweden
- Landstinget Norrbotten – Sweden

Personal health related products for end consumers are less regulated and more of a recent phenomenon but with rapid growth in countries like USA and Great Britain. Thus far there are few Swedish examples. A US example is Jawbone, which has developed a wristband and app that tracks how you sleep, move and eat.

5.13 Healthcare facility products and adaptations as well as single-use products

This business segment is diversified with various products used in the healthcare sector being developed. There are eight companies with more than 100 employees listed in the table below.

Table 9 Companies in the 'healthcare facility products and adaptations as well as single-use products' business segment with more than 100 employees in 2012

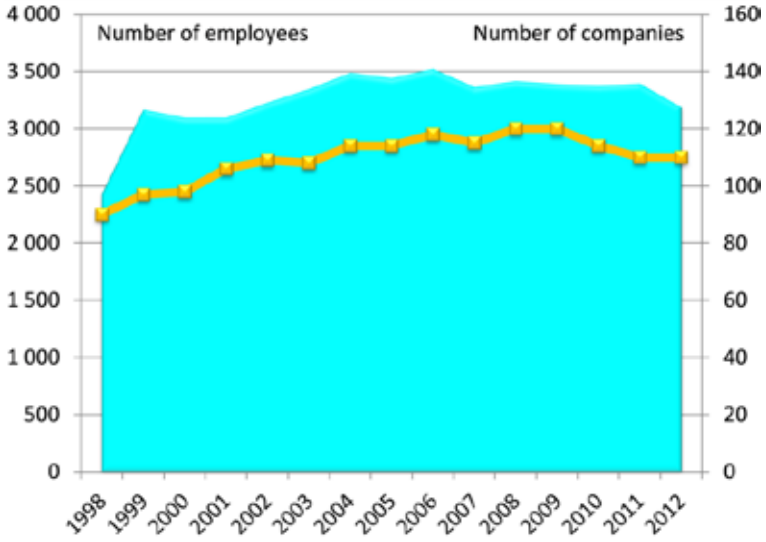
COMPANY	NUMBER OF EMPLOYEES	AREA	LOCALISATION
GETINGE STERILIZATION AB	384	Sterilisation/disinfection/ infection control	Halland
MÖLNLYCKE HEALTH CARE AB	350	E.g. wound care	Västra Götaland
ATTENDS HEALTHCARE AB	293	Incontinence products	Jönköping
GETINGE DISINFECTION AB	249	Sterilisation/disinfection/ infection control	Kronoberg
ARJO HOSPITAL EQUIPMENT AB	166	E.g. hygiene systems	Skåne
LIKO AB	139	Patient transfer aids (sold to US Hill-Rom in 2008)	Norrbotten
AMO UPPSALA AB	135	Eye surgery products	Uppsala
FINESS HYGIENE AB	108	Incontinence products	Östergötland

One large company in this field which has not been included in the analysis is SCA Hygiene Products. The company produces incontinence care products but it is also developing tissue products such as baby diapers and feminine hygiene products. Thus the proportion of the more than 1800 employees which are producing incontinence care products used in the healthcare

[68]Jerlvall L. and Pehrsson T. "eHälsa i landstingen" SLIT-gruppen (2013)

system is not included in the present study. The number of employees for SCA Hygiene Products has grown by more than 600 since 1998.

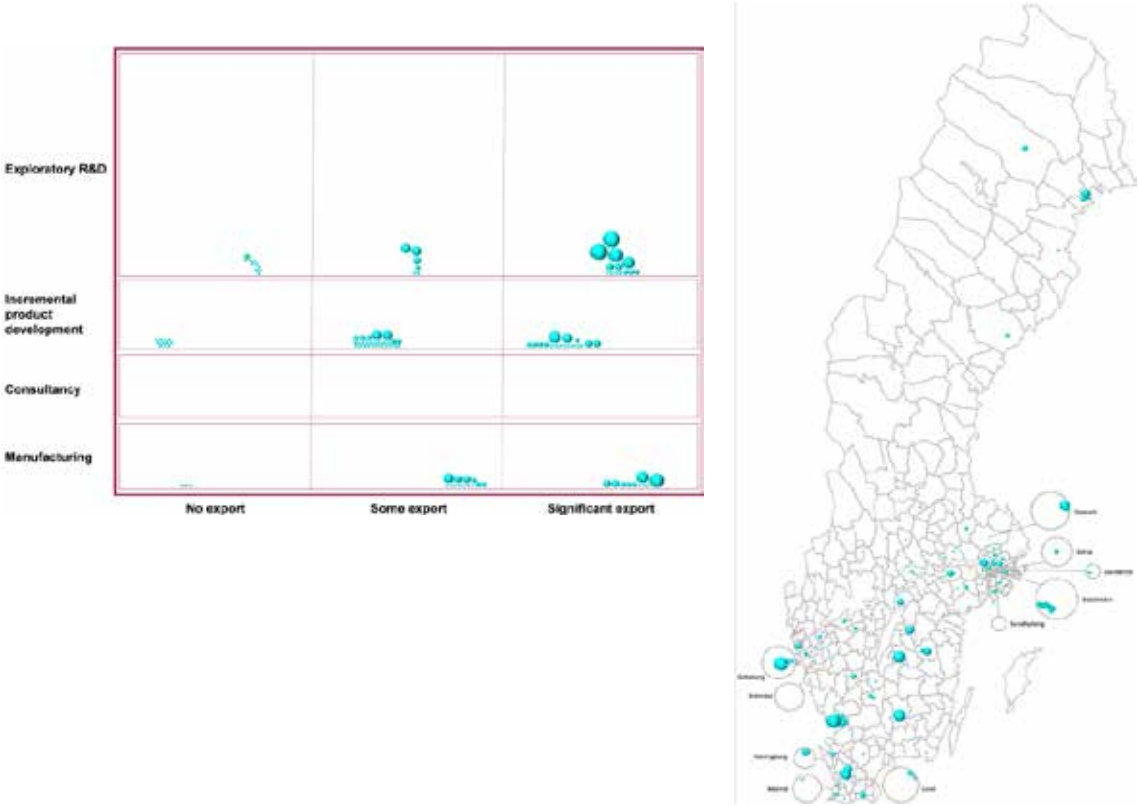
Figure 50 Number of employees of the 'healthcare facility products and adaptations as well as single-use products' business segment (turquoise surface) and the number of companies (orange line) years 1998-2012



In total the business segment had about 3 200 employees in 110 companies in 2012. Since 1999, the employment has been ranging between 3 000 and 3 500 and the number of companies has stayed between 95 and 115. The companies in dental products are all small, seven companies with between 10 and 20 employees and a few micro-sized companies. Becton Dickinson Infusion Therapy in 2012 closed its production unit which had almost 390 employees in 2009.

The companies in this business segment are more distributed geographically than for most other segments. Many of the companies have significant export and the ones without export are primarily micro-sized. About the same number of companies is involved in exploratory R&D as in incremental product development. Most of the companies include manufacturing units. There are more manufacturing units than is indicated by the number bubbles in the manufacturing activity category in Figure 51. This is due to them also including R&D or product development so that the bubbles are found in those categories.

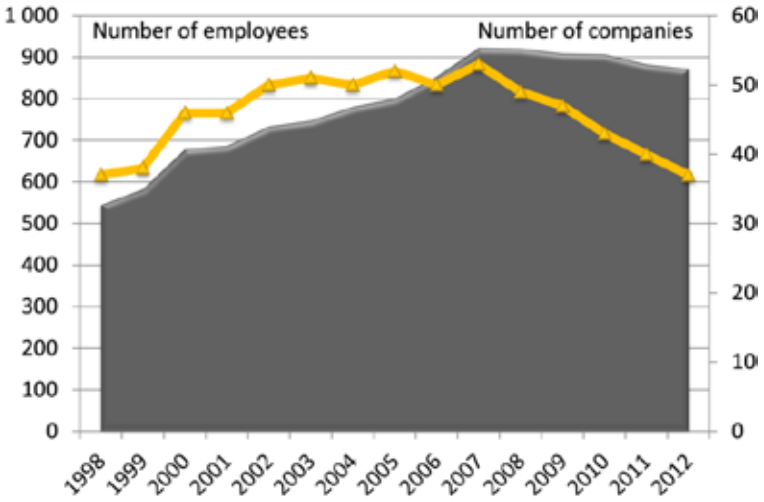
Figure 51 Companies in the 'healthcare facility products and adaptations as well as single-use products' business segment in Sweden in 2012, shown in the bubble diagram as well as geographically distributed according to the location of company facilities



5.14 Assistive products for persons with disability

The companies identified in this category may be somewhat underestimated especially in the early years of the studied time period since the business segment was not included in the database until 2009. The largest company is Permobil, developing electric wheelchairs, with almost 250 employees and located in Sundsvall. Etac Supply Center is the second largest company with almost 100 employees and developing products such as manual wheelchairs, power wheelchairs and transfer products and hygiene systems. There are 17 companies with between 10 and 60 employees in areas like acoustic systems and orthopaedic devices. In total the business segment include almost 900 employees in 37 companies and has grown by about 330 since 1998.

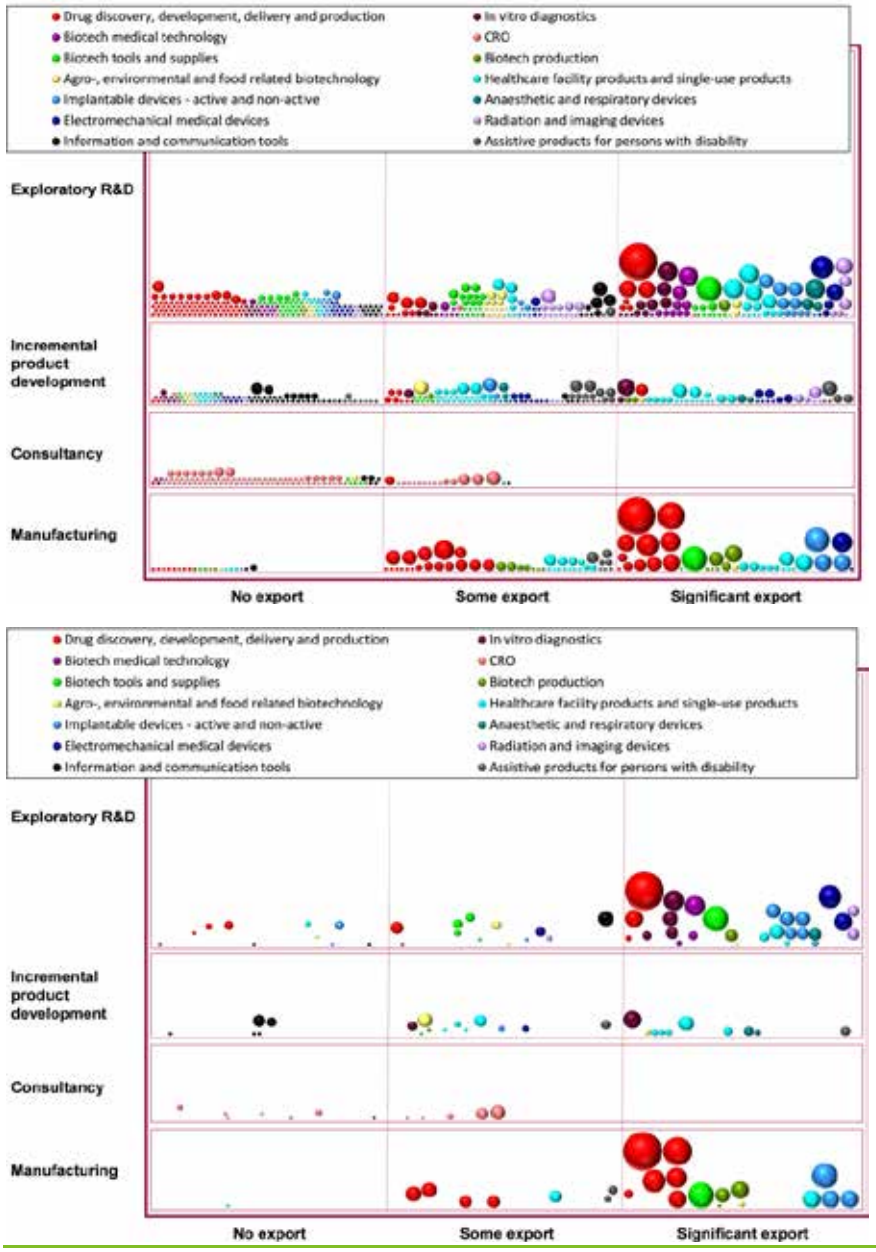
Figure 52 Number of employees of the 'assistive products for persons with disability' business segment (grey surface) and the number of companies (orange line) years 1998-2012



6 Parent company nationality

Foreign-owned life science companies, in terms of parent company nationality, are often large companies active in R&D and/or manufacturing. The consultancy sector is underrepresented among foreign-owned companies. Exports in the consultancy area most often means establishing a site working with the local market and is thus not seen in the trade statistics as export. About 61 percent of the employees in the life science industry are working in companies with a foreign parent company and about 14 percent of the companies are foreign-owned.

Figure 53 Bubble diagrams showing the total life science industry (excluding sales and marketing. Top) and the part of the industry belonging to foreign-owned companies (in terms of parent company nationality. Bottom)



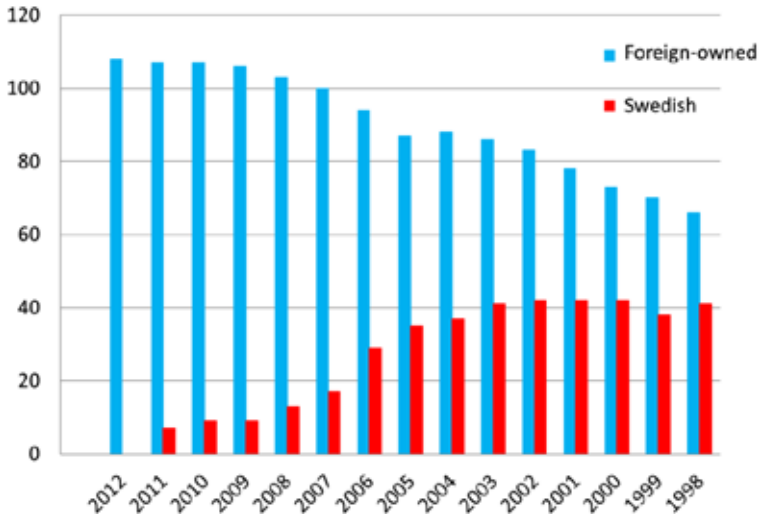
Of the 108 foreign-owned companies in 2012, 37 are US-owned, twelve with ownership in the Netherlands, eight British, six Danish, seven Swiss and five are Luxemburg-owned. As many as 16 other nationalities are found. Medical technology has the most foreign-owned companies, 58, of which 23 are US, six are British and six have their ownership in the Netherlands. Eleven of the Pharmaceutical firms are US-owned and five have their ownership in the Netherlands. Also, British and Danish parent companies own three companies each. In terms of number of employees, British ownership dominates due to AstraZeneca. Among the foreign-owned biotech companies, parent companies from the US are well-represented and include GE Healthcare Biosciences (origin in Pharmacia).

Pfizer, Dentsply (previously Astra Tech), Phadia (recent acquisition by Thermo Fisher), Hemocue, Cepheid (previously Sangtec Molecular Diagnostics) and St Jude Medical are all US-owned. Parent companies in the Netherlands own Qpharma, Crucell and Philips Digital Mammography. Parent companies in Switzerland own Octapharma and Q-Med, and Rechon Life Science (previously Ferring in Malmö) has a Chinese parent company. Cochlear Bone Anchored Solutions (previously Entific) is Australian and Compugroup Medical German. The largest British-owned companies besides AstraZeneca are Attends Healthcare Sweden and Quintiles.

Few foreign acquisitions have led to the closing of the Swedish operations but there are some examples. Carmel Pharma is closing its Swedish operation after being acquired by US Becton Dickinson, St Jude Medical is closing the pacemaker operations and Becton Dickinson is also closing the manufacturing unit in Skåne. An earlier example is DSM Anti-infective which closed its manufacturing unit in Strängnäs in 2008. Siemens Elema closed the x-ray division in Sweden (2003) but divested the life support system and pacemaker parts so that those operations continued in Sweden under the ownership of Getinge (2003) and first US Pacesetter in 1994 and later St Jude Medical, respectively. Some acquisitions have on the other hand led to increased operations, for instance Octapharma, Fresenius Kabi and HemoCue.

The number of companies with a foreign parent has been increasing over time. Figure 54 shows how the 108 companies with a foreign parent company in 2012 have shifted from being Swedish to becoming foreign-owned over the years. Over 60 percent of the 108 companies being foreign-owned had employees also in 1998. Of those, 62 percent had a foreign parent company already then. The number of foreign-owned companies stayed fairly constant until 2003, at which point foreign ownership started to increase, with 2006 and 2007 being the years with the sharpest decrease in the proportion being Swedish.

Figure 54 Number of companies with employees in the years 1998-2012, broken down by foreign-owned (blue) and Swedish (red). N.b. the 108 foreign-owned companies identified in 2012 were the basis of the time series

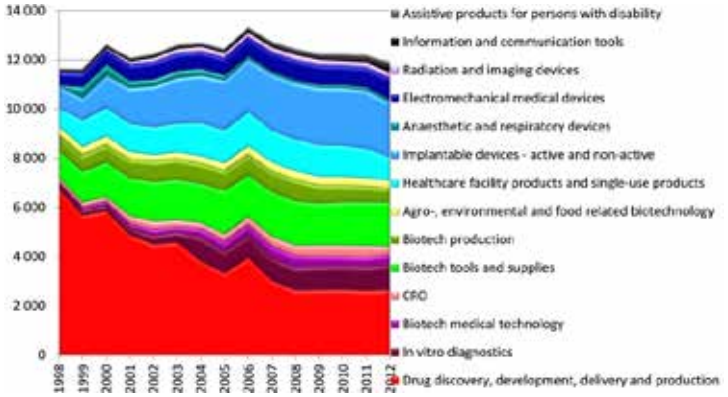


Of the companies with employees in 2012 and with Swedish ownership, about fifteen have, at some point had a foreign parent company in countries such as Switzerland, Netherlands, Luxemburg, Virgin Islands, Austria, Denmark, USA, Norway and Germany.

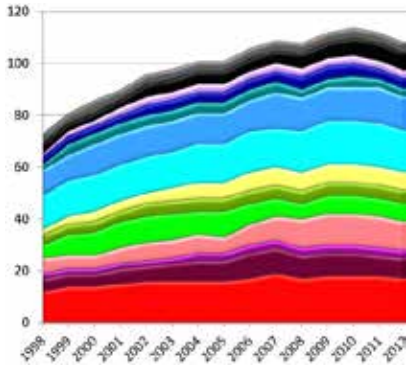
In Figure 55 the development of the number of employees for the companies being foreign-owned in 2012 is shown (excluding AstraZeneca). The steep decrease for drug discovery is due to the divestments and closure of business units from previous Pharmacia (see also Section 8.2). As is seen, the foreign-owned companies have grown in terms of employees in most other business segments. Some of the growth is due to that the above mentioned business units with origin in Pharmacia are entering the group after being divested to a foreign parent company, e.g. Phadia and AMO. The number of foreign-owned companies has increased in all business segments but assistive products for persons with disability. It is especially clear in the drugs segment, for CROs and in agro-, environmental and food related biotechnology, with an increase by five foreign-owned companies each, 1998-2012.

Figure 55 Number of employees and companies with employees each year for the 108 companies being foreign-owned in 2012 (excluding AstraZeneca)

NUMBER OF EMPLOYEES



NUMBER OF COMPANIES

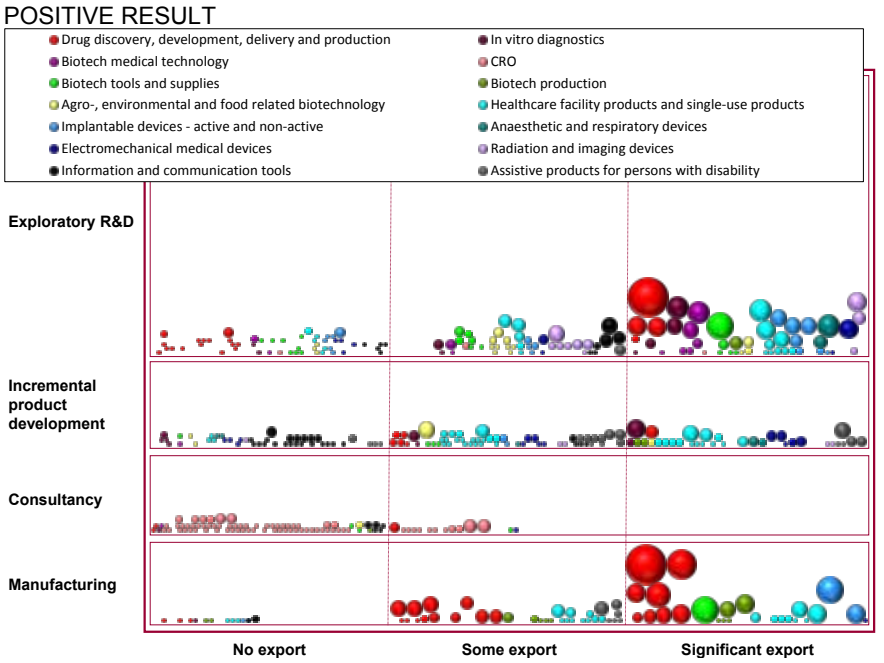


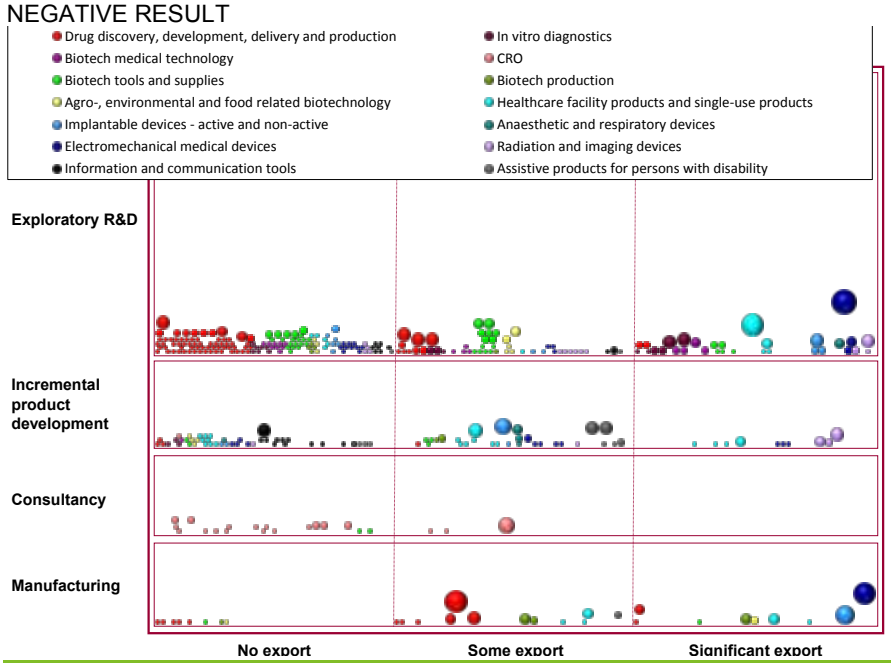
What we have not captured in the present analysis of foreign ownership are the companies which are immediately closed after being acquired.

7 Business results

To understand the economic performance of an industry, it is interesting to know the structure regarding issues such as results after financial items, net turnover and also value added. The graphs below show the corporate population showing positive or negative relative results.

Figure 56 Bubble diagrams showing the companies in the life science industry (excluding sales and marketing) having a positive results after financial items (top) and a negative results after financial items (bottom) in 2012





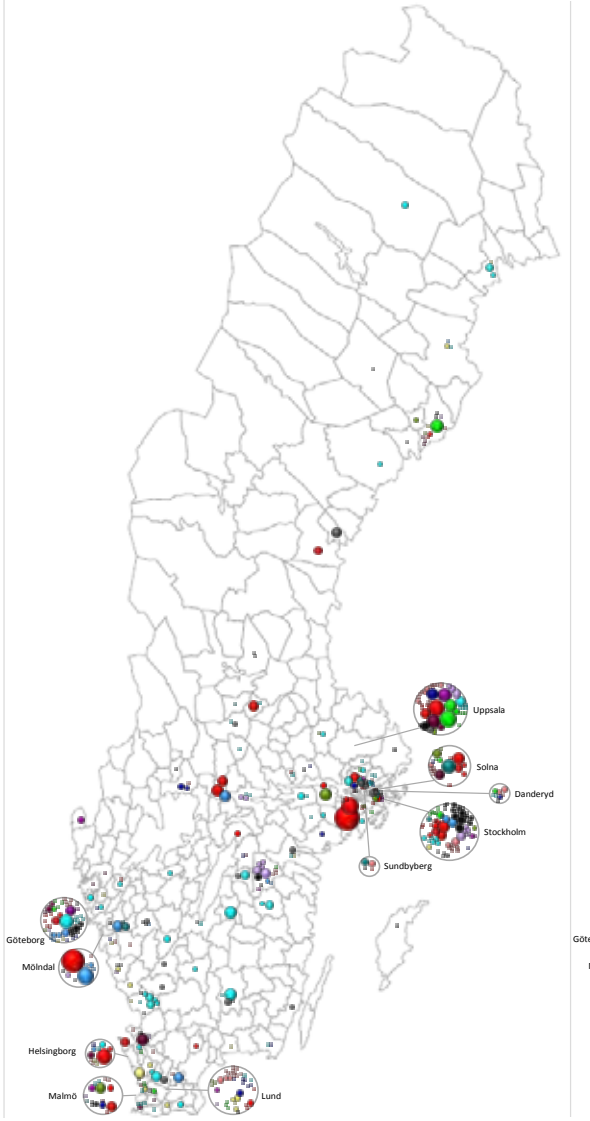
The graphs give a snapshot of the relative results of individual companies in 2012. The results vary over time but also for earlier years the vast majority of employees are found in companies showing positive relative results. The results clearly show the difficulty that recently started micro-sized companies often have in showing positive relative results. Concerning business segments, there is no striking difference in the distribution among those. The many drug discovery and biotech tools and supplies companies with exploratory research are however overrepresented among the companies with negative relative result. It is also clear that a majority of the CROs are showing a positive relative result, as well as the contract manufacturing organisations (CMOs) in red. Almost all of the foreign-owned companies are showing positive results.

A previous study[69] analysed how the proportion of the corporate population showing positive or negative relative results changed over time in different size classes of the industry. On average, 54 percent of the micro-sized companies had negative relative results years 2005-2009. For small-sized companies the proportion was been fairly constant with 53 percent showing positive results years 2005-2009. For the medium-sized companies the variation over the years was greater with an average of 74 percent of the companies showing positive results years 2005-2009.

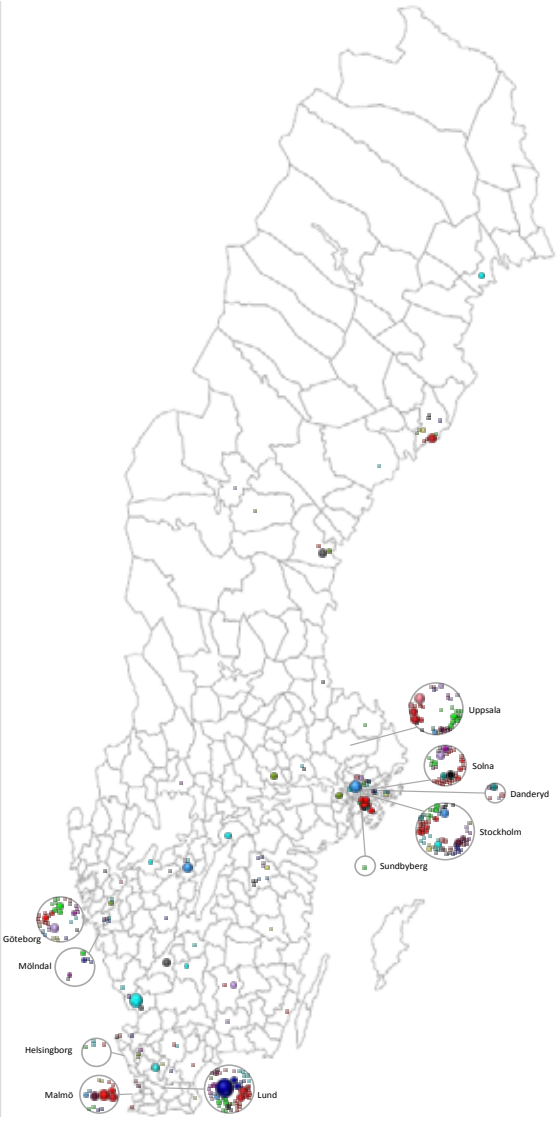
[69] Sandström A. Dolk T. and Dolk B. "Life Science companies in Sweden - Including a comparison with Denmark" VA 2011:03 VINNOVA (2011)

Figure 57 Map showing the companies in the life science industry (excluding sales and marketing) having a positive results after financial items (left) and a negative results after financial items (right) in 2012

POSITIVE RESULTS



NEGATIVE RESULTS

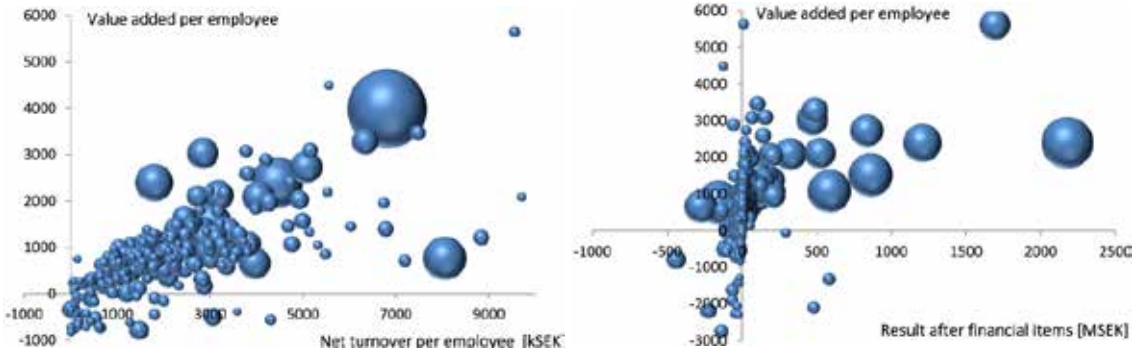


As the location of many small drug discovery companies, Stockholm/Uppsala and Malmö/Lund is also home to many companies with negative results. As would be expected, almost all companies with low net turnover have negative results.

In Figure 58 some other financial indicators are visualised for the life science industry (excluding sales and marketing): value added per employee (excluding one company with much higher value added than shown in the graph), net turnover per employee (excluding six companies with much higher value than shown in the graph) and result after financial items (excluding AstraZeneca with a much higher value than shown). The data is shown for companies larger than four employees. There is a correlation between value added and net turnover per employee. Of the 308 visualised companies 76 have a result after financial items

ranging between SEK +2 and -2 million. The fluctuation over time means that many of the companies switch back and forth regarding whether they have positive or negative result after financial items.

Figure 58 Value added[70] per employee combined with net turnover per employee (left) and results after financial items (right) for life science companies with more than four employees [the bubble size (volume) is proportional to the number of employees]



[70] Total value added means summing the value added per unit over all units sold. Total value added is equivalent to revenue less outside purchases (of materials and services). Value added is a higher portion of revenue for integrated companies, e.g., manufacturing companies, and a lower portion of revenue for less integrated companies, e.g., retail companies.

8 Astra- and Pharmacia-related companies in Sweden

As previously mentioned, the Big Pharma companies AstraZeneca (in Sweden with an origin in Astra) and Pfizer (in Sweden with an origin in Pharmacia) have become less and less dominant in the Swedish life science industry in terms of employment. In this chapter some facts regarding the companies originated in Astra and Pharmacia is found.

8.1 Astra-related companies

Swedish Astra activities spun out or divested

Medivir was formed in 1988 based on a virology project that was going to be closed[71]. In 2012 Medivir had 75 employees, including its subsidiaries. The company has a focus on infectious diseases, especially hepatitis C. Medivir has launched a new drug against cold sores on the market and has seven projects in pipeline in collaboration with external partners. A project regarding hepatitis C is in phase III.

Another spin-off is Cobra biologics, the AstraZeneca biotech production facility in Södertälje, which was acquired by Swedish Recipharm in 2007. The company is a CMO, manufacturing monoclonal antibodies, recombinant proteins, DNA, viruses, phage and cell line derived products as well as pharmaceuticals for clinical trials and commercial supply. The company has also acquired a production unit in Matfors outside Sundsvall and in 2012 had 73 employees.

Albireo is the third spin-off being formed (in 2008), active in the gastrointestinal area. The company had eight employees in 2012 and has six preclinical projects, one project in phase two and one project in phase three. The company brought several preclinical projects and one clinical project from AstraZeneca when it was formed. The company has attracted foreign venture capital[72]. The company's activities are performed in a complex network of consultancies and collaborative partners piecing together the puzzle that forms the most often iterative pharmaceutical innovation process. Today the company has formed partnership agreements with Japanese Ajinomoto and Danish Ferring regarding the phase three project.

In 2011, AstraZeneca divested its medical technology operations, Astra Tech, to US Dentsply. Astra Tech operations included dental implants and urological and surgical products in Gothenburg. In 2013 Dentsply formed the subsidiary Wellspect HealthCare AB containing the urological and surgical products whereas the implants is part of Dentsply AB. Wellspect HealthCarre include products such as the hydrophilic catheter introduced in 1983 and solutions for the postoperative drainage, collection, filtration and reinfusion of autologous blood.

[71] STU, a predecessor of VINNOVA gave a substantial grant when the company was formed
[72] Phase4 Ventures, TPG Biotech, TVM Capital and Scottish Widows Investment Partnership (SWIP)

Since the closing of the R&D units in Lund and Södertälje some of the previously employed have started new businesses[73]. Many of those are not in the life science field but completely other branches of industry. Of the new ventures in life sciences a vast majority are consultancies offering the expertise of the employees for organisational/managerial issues, contract research or concerning regulatory issues with examples such as LabJoy, Truly Translational, Gerik Medical Consulting and Novandi Chemistry. Few are devoted to themselves developing new medicines, with Northern Light Pharmaceuticals as one exception. It is still too early to analyse how many are employed in these companies since most of them have not yet submitted an annual report to Swedish Companies Registration Office (Bolagsverket).

AstraZeneca globally

Since the merger of Swedish Astra and British Zeneca in 1999, several hive-offs, investments, acquisitions and establishments have taken place. Many of the investments from 1999-2007 were made in UK and Sweden. The investments included opening and expanding several R&D and manufacturing facilities in the UK and opening research laboratories in Boston, USA, a manufacturing plant and a clinical research unit in China and new R&D facilities in India and Canada. There were also manufacturing facilities in France and Egypt, as well as acquisition of a controlling stake in Astra-IDL in India. AstraZeneca sold its penicillin factory in Strängnäs to Recip in 2001 but has invested in the production facility in Södertälje. From 2005-2007, AstraZeneca acquired KuDos Pharmaceuticals, Cambridge Antibody Technology, Arrow Therapeutics (anti-viral therapies), the US-company MedImmune (a USD 15.2bn deal in 2007 to strengthen AstraZeneca in the biopharmaceutical area), a biologics manufacturing facility in Canada (from DSM Biologics) and French Novexel (infection research). With these acquisitions, the AstraZeneca pipeline broadened into biopharmaceuticals and added bioproduction capabilities. AstraTech acquired Cresto Ti Systems in 2005.

In 2007, AstraZeneca opened a process and development laboratory next to its R&D centre in Bangalore, India and its first clinical pharmacology unit in Shanghai, China. The Shanghai R&D unit, had a focus on clinical research and clinical trials but also some discovery research in the cancer, respiratory/inflammation and renal areas. The focus in China has been on knowledge about Chinese patients, biomarkers and genetics, initially with a specific focus on cancer. The R&D unit in Bangalore, had a focus on infection, especially tuberculosis. In the same year, AstraZeneca boosted investments in the R&D centre in Boston, US (infectious disease area and cancer) and the process R&D unit in Macclesfield, UK. In recent years, AstraZeneca has for instance invested in collaboration with the PET-centre at Karolinska Institutet and has been collaborating with Region Skåne on chronic obstructive pulmonary disease and Columbia University Medical Center in New York on diabetes and obesity. AstraZeneca has also had strategic collaborations with Big Pharma companies such as Abbott and Merck on specific projects as well as collaboration with the commercialisation company for the UK's Medical Research Council to share access to the AstraZeneca collection of compounds.

[73] Life Science Sweden identified as many as 69 in the spring 2013

In recent years a number of R&D units in neuroscience have been closed. This includes Södertälje (SE) with about 1 200 R&D personnel, Montreal (CA) 150 employees and Wilmington (US), about 1 000 employees. Also, the earlier focusing of R&D in the respiratory, inflammatory and autoimmune disease areas to the Gothenburg site meant a closing of the R&D units in Lund with about 900 R&D personnel (SE) and Charnwood (UK), with about 1200 employees. In addition to these changes also the R&D activities in Avlon (UK) was closed (about 150 employees in areas like pharmacology and process development) whereas manufacturing remains in the Avlon site. The Mölndal site has expanded and has become a global centre for the following therapeutic areas: cardiovascular, gastrointestinal, respiratory and inflammatory diseases.

AstraZeneca in 2013 announced continued changes to its R&D organisation focusing R&D to three strategic R&D centres in Cambridge (UK), Washington/Gaithersburg (US) and Gothenburg/Mölndal (SE). The prioritised areas are cancer, cardiovascular/metabolic disease, respiratory, inflammatory and autoimmune disease. Alongside this, AstraZeneca will remain active in infection and neuroscience with targeted investments in opportunities and collaborations. In 2014 AstraZeneca announced its closing of the R&D unit in Bangalore today focusing on tropical medicine, malaria and tuberculosis affecting 168 employees. Many of the programmes will be transferred to AstraZeneca's UK-based R&D operations in Macclesfield as well as to outsourcing partners.

All together more than 30 000 jobs have been lost in AstraZeneca since 2007. At the same time the company continues to acquire biotech firms such as and Ardea Biosciences (cancer and gaut), Pearl Therapeutics (respiratory) and Omthera (cardiovascular). AstraZeneca has also announced new partnering deals. For example an agreement with Moderna Therapeutics to discover, develop and commercialise messenger RNA therapeutic for the treatment of cardiovascular, metabolic and renal diseases as well as cancer. Messenger RNA therapeutics, is a new treatment approach that enables the body to produce therapeutic protein in vivo, opening up new treatment options. Moderna received an upfront payment of USD 240m and will be entitled to an additional USD 180m when achieving three technical milestones. The continued acquisitions of, and partnering with biotech companies is part of a global trend for the Pharma industry as has been described in previous chapters. AstraZeneca has also announced an agreement under which AstraZeneca will acquire the entirety of Bristol-Myers Squibb's interests in the companies' diabetes alliance.

In total the AstraZeneca sales have gone down with 21 percent in the US in 2012 and with 19 percent in Western Europe whereas emerging markets grew by 4 percent. Comparing revenues in 2012 with 2013 the sales went down by six percent.[74] An example of a recently launched drug by AstraZeneca is Brilinta. Brilinta reduces the rate of heart attack (myocardial infarction) and cardiovascular death in adult patients with acute coronary syndrome. The drug is now approved in 88 countries, including in the European Union, the US, Brazil, Canada, Australia and Russia, and is under review in 23 countries. The drug is reimbursed in 29, available in 33 patient pay markets and commercially launched in 82 countries. Sales in 2012 were USD 89m.

[74] Annual report 2012 and 2013

The AstraZeneca top ten drugs in terms of sales however, generated sales between 866 (Pulmicort) and USD 6 253m (Crestor) each. For Brilinta it is early days and AstraZeneca in its annual report 2012 state that Brilinta has the potential to become a major product for AstraZeneca but that the market uptake thus far has been slower than expected. Brilinta competes with Plavix from Bristol-Myers Squibbs and Sanofi-Aventis. The loss of patent rights for Plavix in 2012 is also likely to adversely affect the growth of Brilinta which is in the same product class.

8.2 Pharmacia-related companies

When previous Pharmacia operations were downsized, divested or closed, primarily in Stockholm and Uppsala, the rest of the life science industry was expanding. AstraZeneca, some of the divested business units with origin in Pharmacia as well as a number of start-up companies were employing. Pharmacia alumni have brought their industrial competence to life science companies throughout the country, or become employed in for instance venture capital companies and at public organisations in the life science innovation system. Managing a small venture capital financed firm in early stage with a high burn rate is however different from the conditions for operations in a large corporation. The access to this human capital has by many analysts been seen as one success factor behind the development of especially the Uppsala life science cluster.

Pharmacia time line

1911: Pharmacia formed.

1990: Pharmacia acquired by Procordia and merges with Kabi under the name Kabi Pharmacia. Subsequent name change to Pharmacia.

1995: Pharmacia merges with Upjohn to form Pharmacia & Upjohn. The company has approximately 7 000 employees in Sweden.

1996: Pharmacia Biosensor is sold and becomes Biacore.

1997: Pharmacia Biotech is merged with British company Amersham and in 2001 is named Amersham Biosciences.

1997 Pharmacia has 5 249 employees.

1998: Pharmacia closes its research unit in Lund and major sections are purchased by Active Biotech.

The same year, German company Fresenius takes over production of nutrient solutions and now operates under the name Fresenius Kabi.

1999: Pharmacia & Upjohn merges with Monsanto. The new group calls itself Pharmacia Corporation.

2001: Most of the remaining research within Pharmacia in Sweden is sold off and the new company Biovitrum is formed. Biovitrum subsequently sells the substitute plasma operation to

Swiss company Octapharma. The same year, the clinical trials operation is acquired by Quintiles. In 2006 iNovacia, is formed as a management buy-out from Biovitrum.

2002: Pfizer acquires Pharmacia.

2003: Pfizer sells Pharmacia Diagnostics to two venture capital companies (corporate group now called Phadia and acquired by Thermo Fisher Scientific in 2011).

2004: Amersham Biosciences is sold to the American company General Electric Inc. and is now GE Healthcare Bio-Sciences.

2004-2007: Pfizer invests to increase the production capacity in the bioproduction plant in Strängnäs. Bangalore-based pharmaceutical company Kemwell completes acquisition of Pfizer's Salazopyrin manufacturing plant in Uppsala. Advanced Medical Optics acquires the ophthalmic surgery operation and Pfizer moves its Uppsala operation to Stockholm.

In 2006, the Helsingborg production unit (Pfizer Consumer Healthcare) manufacturing the Nicorette product family is sold to the Johnson & Johnson group to form McNeil Sweden AB. Pfizer also closes its production unit in Stockholm.

2008-2010: GE Healthcare Bio-Sciences acquires Biacore.

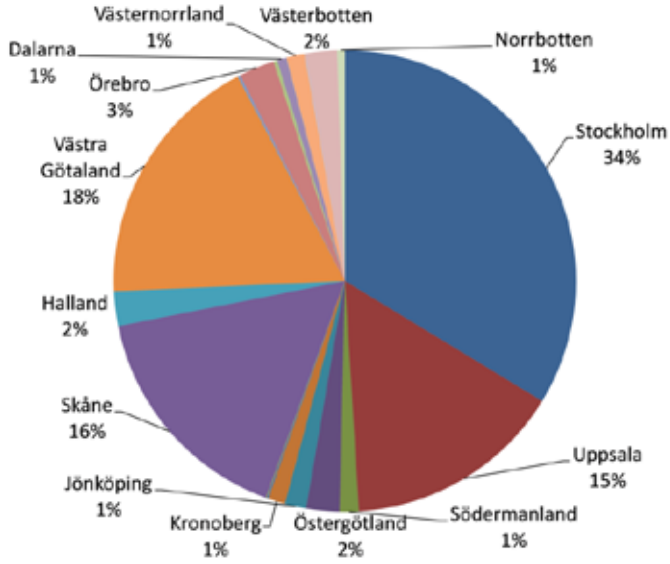
Not all Pharmacia-related operations have been closed or divested. There is also an example of operations being integrated in academia, the Chemical Biology Consortia Sweden, with the Karolinska Institutet node originating in Pharmacia. Pfizer currently has no own research facilities left in Sweden but the corporation has continued to invest in the biotech production unit in Strängnäs.

Since 1995, the former Pharmacia operation has been sold to various owners and in 2009 comprised 13 companies/corporate groups. Between 1997 and 2009 these companies jointly decreased their number of employees by some 12 percent, to about 5 840 in total, corresponding to a decrease of about 770 employees. Since the dynamics in the group of companies with an origin in Pharmacia has continued with mergers and acquisitions, and their operations have changed over time it has since 2009 become less meaningful to follow their development as a group with a common origin.

9 Swedish Life Science regions

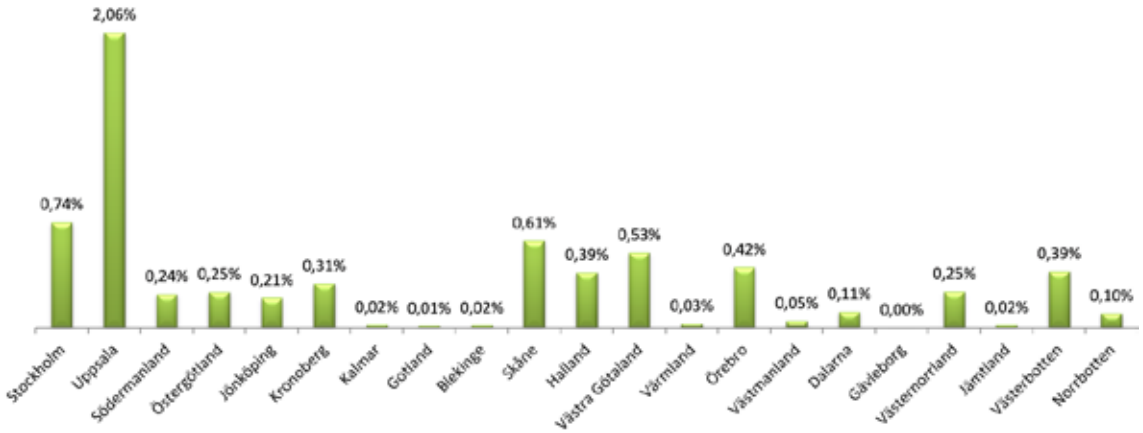
In Figure 59 the proportion of the employment in the Swedish life science industry (excluding sales and marketing) is shown for Swedish counties with more than 0.5 percent of the employment.

Figure 59 Proportion of the number of employees for counties with more than 0.5 percent of the total life science industry employees (excluding sales and marketing)



Stockholm, Uppsala and Södermanland together still hold 50 percent of the employment, despite the downsizing of AstraZeneca and Pfizer. The changes in AstraZeneca Södertälje had however not come completely into effect in 2012. Västra Götaland and Halland together hold 20 percent of the employment and Skåne 16 percent. These are the dominating life science regions in Sweden.

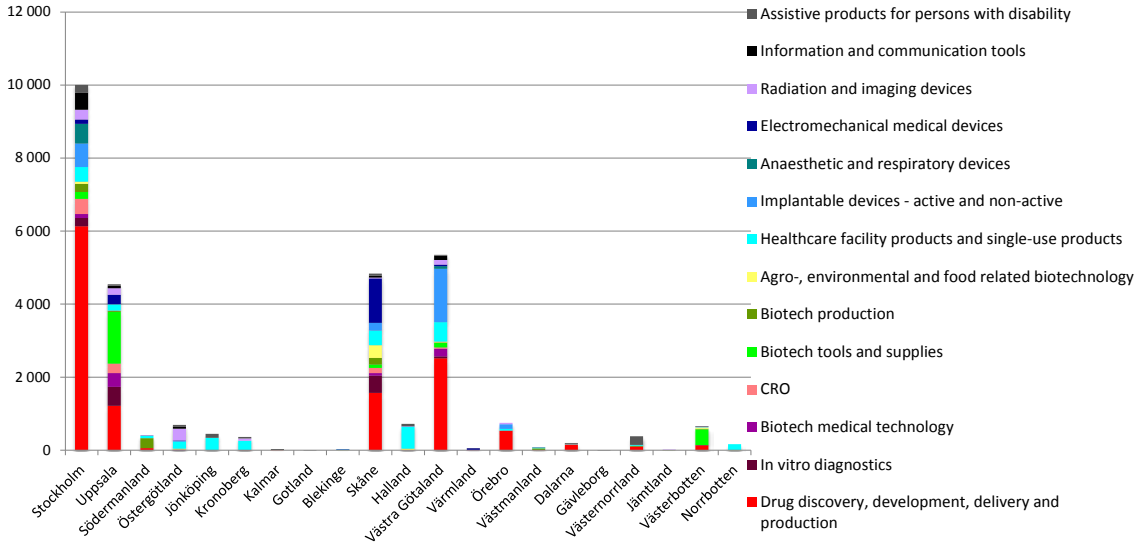
Figure 60 Proportion of the population of the 21 Swedish counties aged 16-64 employed in the Swedish life science industry (excluding sales and marketing)



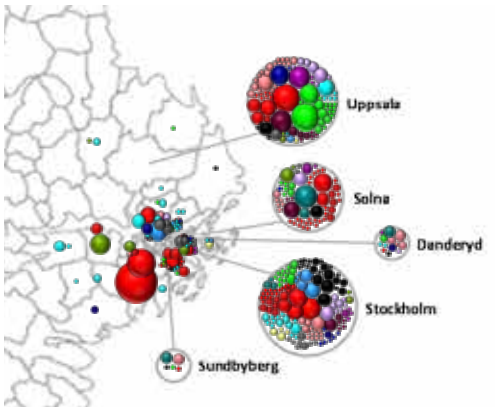
In relation to population aged 16-64, Uppsala has the highest density with over 2 percent of that population employed in the life science industry, and then follows Stockholm, Skåne and Västra Götaland (Figure 60). Thus the employment in life sciences in these regions is not only high in absolute terms but also in relation to population.

In Figure 61, the regional specialisation in the included business segments is shown. The significance of the drugs segment is clear for all major regions and the strong focus on biotech tools in Uppsala as well as the strength in implants in Västra Götaland.

Figure 61 Geographic distribution of the number of employees in the business segments of the life science industry (excluding sales and marketing) 2012



9.1 Stockholm, Uppsala and Södermanland



The companies in Stockholm, Uppsala and Södermanland are visualised according to their location to a municipality in the region and business segment colour. The focus on biotech tools and supplies in Uppsala is clear as well as the many drug discovery and development companies throughout the region. Perhaps less well known are the many CROs and also ICT tools companies located to the region. It is common in many industries that consultancies have a tendency to locate their business to Stockholm. A VINNOVA analysis of the ICT industry

showed that more than 50 percent of that industry is located in Stockholm. The many companies in Solna are often spin-offs from Karolinska Institutet. AstraZeneca still has an R&D bubble besides the bubble for the manufacturing unit in Södertälje since the closing of the R&D unit in Södertälje was not completed until the end of 2012.

Half of the employees in the region work in 'drug discovery, development, delivery and production' in the region, followed by 'biotech tools and supplies' (11 percent), 'in vitro diagnostics' and CROs with five percent of the employment each (Figure 62). Almost a quarter of the companies are in the drugs business segment, 13 percent are CROs, 12 percent healthcare facility products and 11 percent are companies in biotech tools and supplies. Of the employees, 5 900 (40 percent) were employed in units with less than 250 employees and almost 260 of the company facilities were micro-sized in 2012.

Figure 62 Number of employees and company facilities in Stockholm, Uppsala and Södermanland in 2012

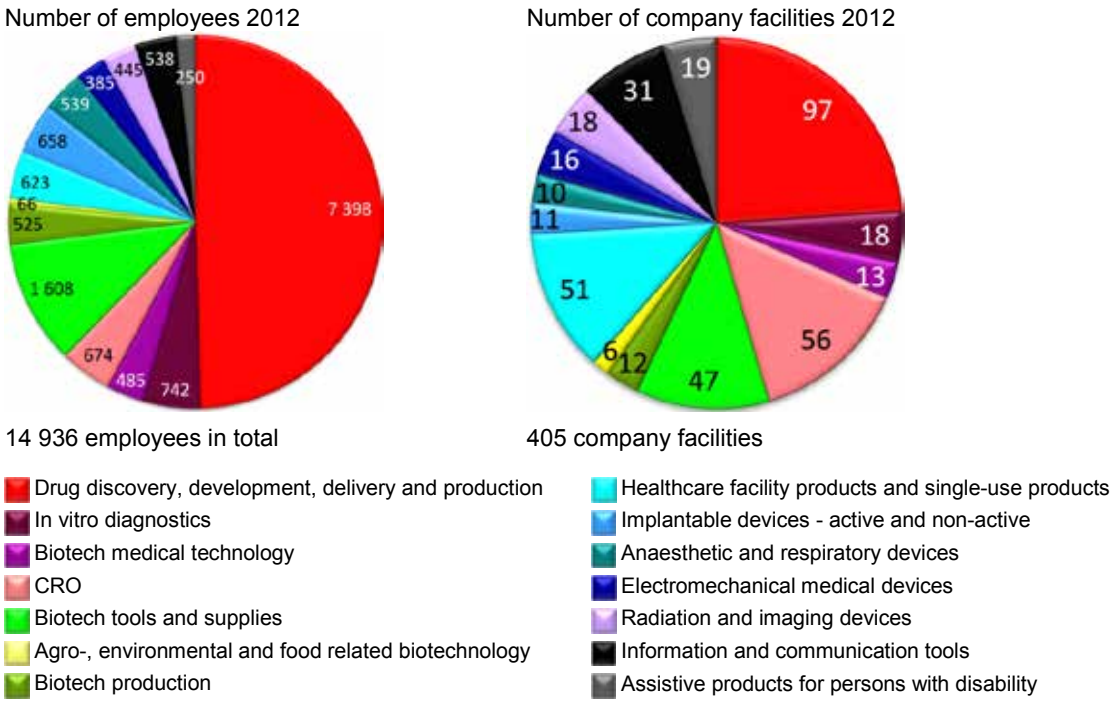
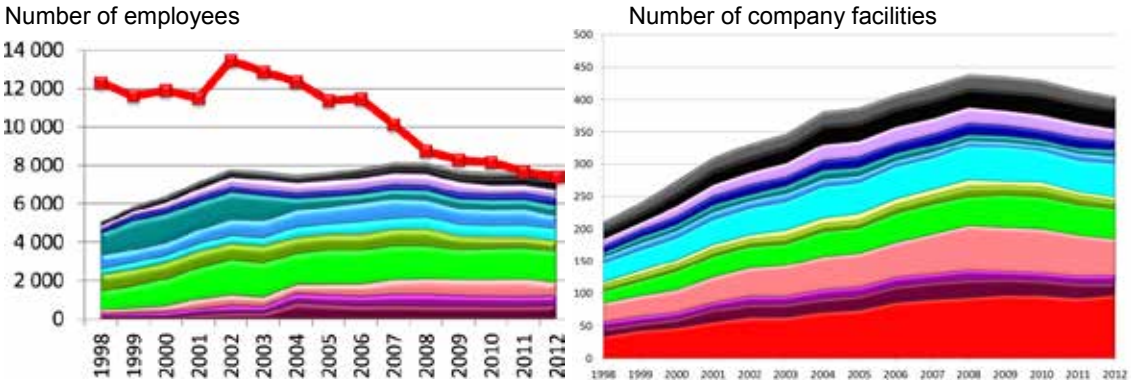
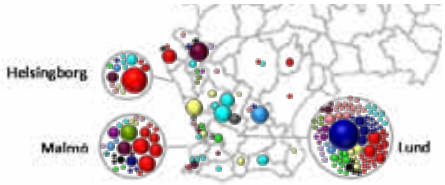


Figure 63 Number of employees and company facilities in the region 1998-2012 ('drug discovery, development, delivery and production' is shown as a red line)



In the diagram showing the development of the employment the drugs business segment is shown as a line since it dominates the trend (Figure 63). Outside that segment the employment in the region has grown by almost 2 500. In the latest three-year period however, the employment has declined by about 600. The number of companies has primarily grown in drugs, CROs, biotech tools and healthcare facility products as well as ICT tools. The total growth in number of companies is over 190. The segment with the largest growth in employment is biotech tools. SMEs which have grown for instance include Oasmia Pharmaceuticals, Olerup, Atlas antibodies, Bactiguard, Cambio Healthcare, Cepheid, Abilia, Compugroup, Olink, Orasolv and Contextvision.

9.2 Skåne



The companies in Skåne are visualised according to their location to a municipality in the region and business segment colour. It is difficult to identify a particular focus area, companies in all business segments are found. The larger companies include Gambro in Lund, McNeil in Helsingborg, Hemocue in Ängelholm and Atos medical in Hörby. There are also a number of companies in the 'agro-, food and environmental biotechnology' business segment such as Syngenta Seeds, Biogaia and Probi as well as several in the healthcare facility products area such as Arjo Hospital Equipment (almost 170 employees) and Arjo Huntleigh (about 70 employees). Getinge in 2013 announced that the Arjo Huntleigh manufacturing unit is to be closed and the production moved to Poland and the closing of the Becton Dickinson unit was finalised 2013. Apart from the manufacturing unit of McNeil with almost 700 employees there are several other pharmaceutical manufacturing units in Skåne, such as Apotek Produktion & Laboratorier with over 200 employees, Qpharma (over 120 employees) and Recipharm Höganäs (almost 80 employees), Bioglan with 60 employees and Rechon with 55 employees. In drug discovery the companies Active Biotech and BioInvent are the two largest with 76 employees

each in 2012 and there are several other SMEs in the drugs business segment. There are also a few companies with core competence in drug delivery such as Camurus and Galenica which combine own drug development with contract services concerning drug delivery to other companies. In vitro diagnostics is a large business segment due to Hemocue with over 300 employees.

About 32 percent of the employees in the region work in the drugs segment followed by electromechanical medical devices (24 percent, primarily due to Gambro), and in vitro diagnostics with 10 percent of the employment (Figure 64). When it comes to the number of companies the picture looks a bit different, with for example, a number of micro-sized CRO companies. The business segment with the highest number of companies is drugs, CROs and healthcare facility products, followed by biotech tools. In total the number of employees was 4 835 in 2012 and had increased by 130 since 1998, despite the closing of the AstraZeneca unit in Lund. In the latest three-year period however, the employment in Skåne has declined by almost 1 510. Of the employees, 2 830 (58 percent) were employed in units with less than 250 employees and more than 130 of the company facilities were micro-sized in 2012.

Figure 64 Number of employees and companies in Skåne in 2012

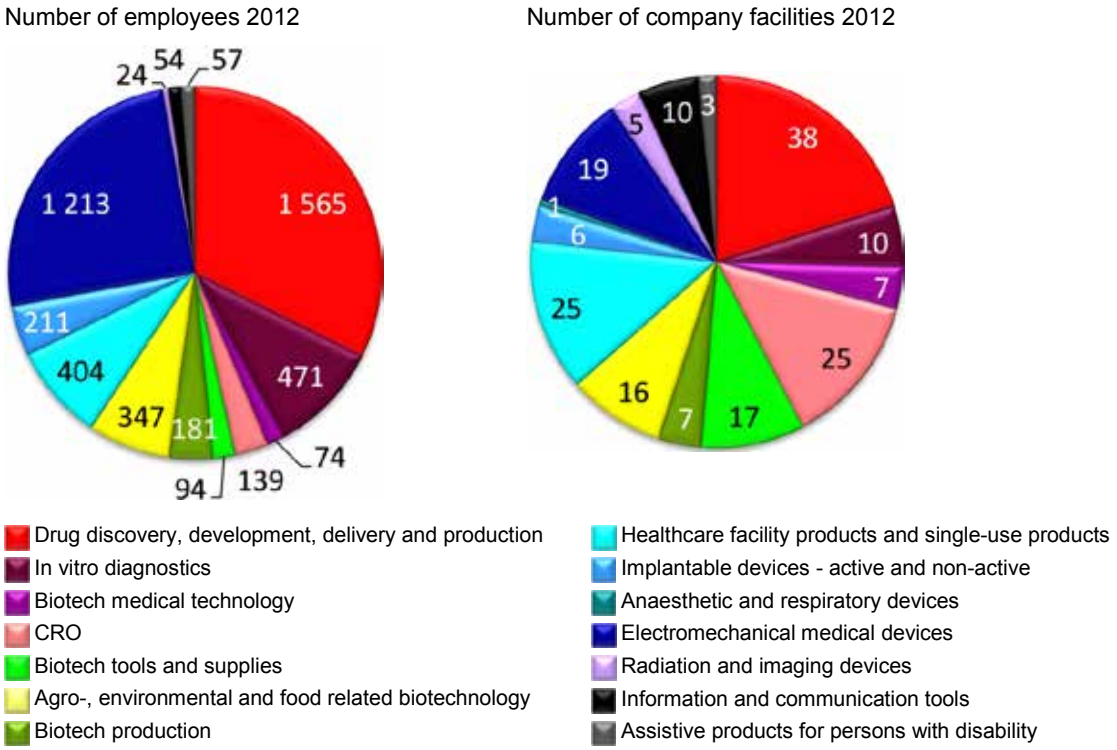
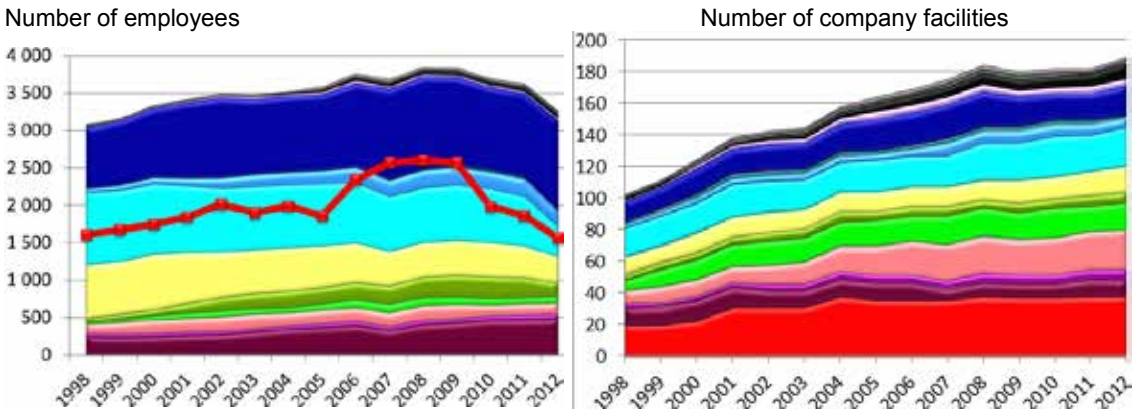
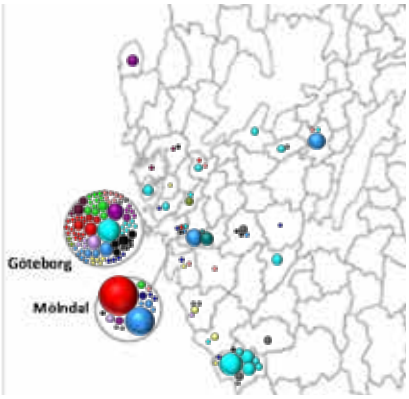


Figure 65 Number of employees and company facilities in the region 1998-2012 ('drug discovery, development, delivery and production' is shown as a red line)



In the diagram showing the development of the employment the decline since the closing of the AstraZeneca unit is clear (Figure 65). The 'agro-, food and environmental biotechnology' as well as 'healthcare facility products' business segments have also declined, by about 360 and 570 employees each. The companies responsible for the decrease are largely Syngenta seeds and Lantmännen Sw Seed as well as Becton Dickinson. The positive development of Hemocue and Gambro has contributed to the increase in 'in vitro diagnostics' and in 'electromechanical medical devices', respectively, and Atos Medical to the implants segment. But also smaller companies have grown such as Polypeptide Laboratories (165 employees in 2012), Biogaia (28), Alligator Biosciences (23) and Camurus (27). The segments with the largest growth in number of companies are drug discovery, development, delivery and production, CROs and biotech tools and supplies. In total the number of companies has grown by 86 since 1998.

9.3 Västra Götaland and Halland



The companies in Halland and Västra Götaland are visualised according to their location to a municipality in the region and business segment colour. The focus on healthcare facility products in Halland is clear as well as the presence of several large companies in implants in Västra Götaland (Nobel Biocare, Cochlear and Dentsply). There are also many spin-off companies from Gothenburg University, Chalmers and Sahlgrenska Academin in several business segments. AstraZeneca and Dentsply are located in Mölndal.

About 41 percent of the employees in the region work in the drugs segment followed by implants (24 percent) and healthcare facility products with 19 percent of the employment (Figure 66). When it comes to number of companies the picture looks quite different. For example, there are a number of micro-sized companies in the agro, food and environmental biotechnology area. The business segment with the highest number of companies is healthcare facility products, followed by drugs, implants and ICT.

In total the number of employees was almost 6 100 in 2012. The employment has increased by 840 in the latest three-year period and by 3 200 over the entire studied time period. Of the employees, 2 080 (33 percent) were employed in units with less than 250 employees and almost 110 of the company facilities were micro-sized in 2012.

Figure 66 Number of employees and companies in Västra Götaland and Halland in 2012

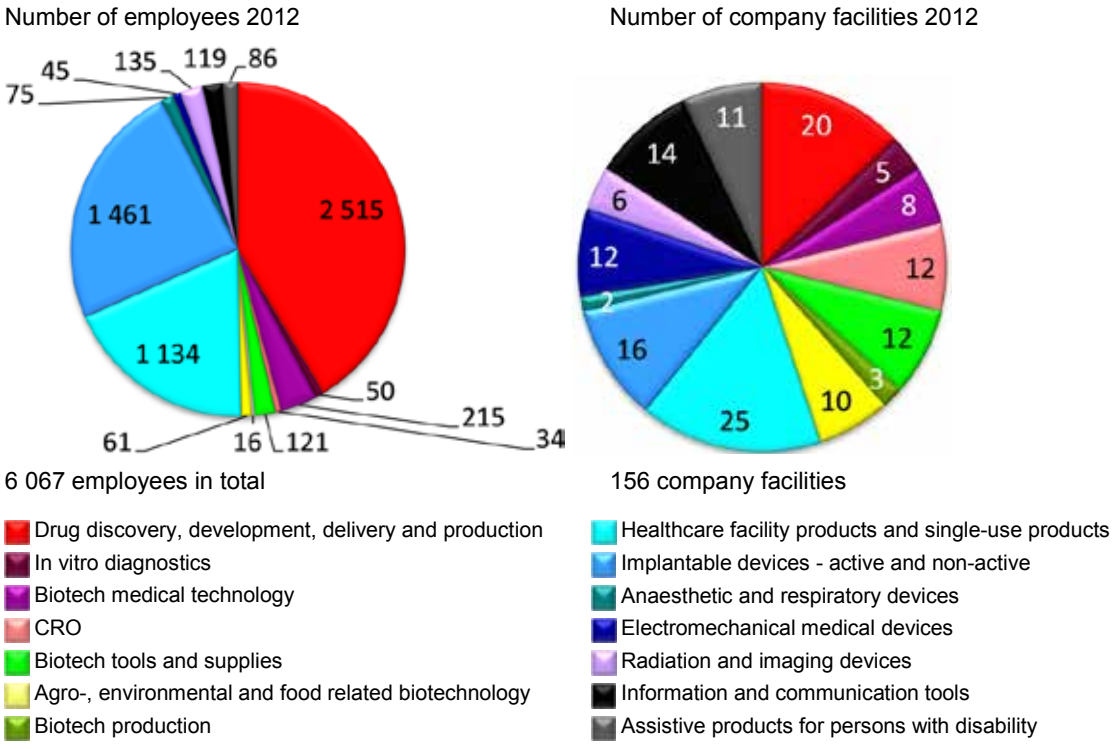
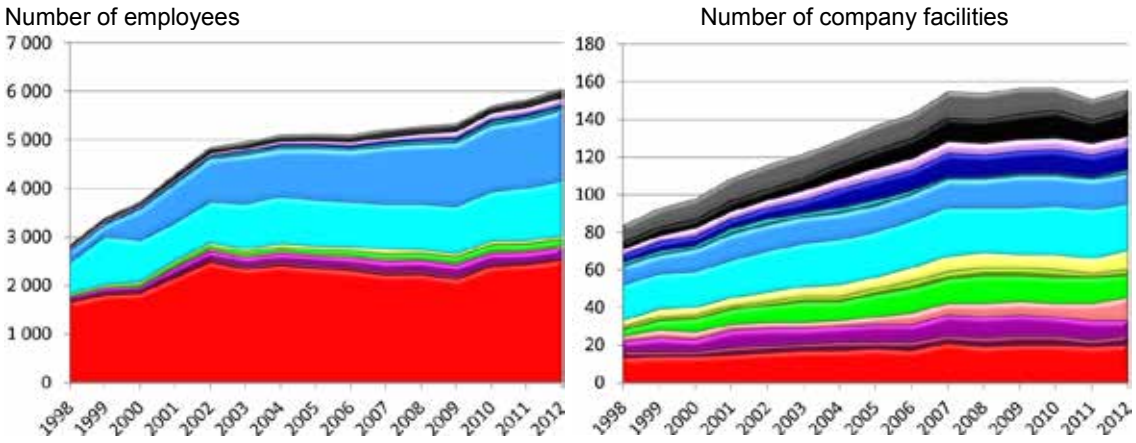
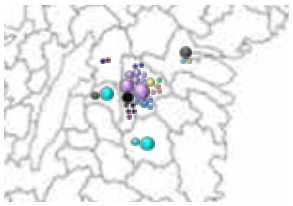


Figure 67 Number of employees and company facilities in the region 1998-2012



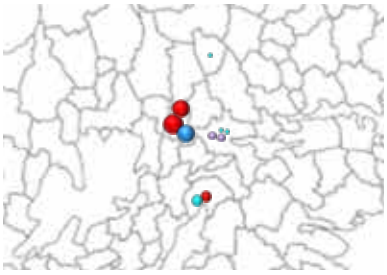
In the diagram showing the development of the employment the growth in the three largest business segments is evident (Figure 67). Companies contributing to the growth include Dentsply, Cochlear, the Getinge group, Mölnlycke Healthcare, Vitrolife and Elos Medtech Timmersdala but also Cellectics, Compugroup Medical and Breas Medical. Eight business segments have grown by six to ten companies each and in total the number of companies has grown by 72 since 1998.

9.4 Other regions: Västerbotten, Örebro and Östergötland



In Östergötland 33 companies with almost 690 employees have been identified in 2012. The number of companies has increased by 17 and the employment has grown by 500 since 1998. In the last five years it is primarily the healthcare facility products segment which has grown, with almost 120 employees. Among the companies which have contributed to the growth in the region are Sectra Imaging IT Solutions, Cambio Healthcare Systems, Finess Hygiene and Elekta.

In Västerbotten there are 654 employed in 28 companies. The largest companies are the manufacturing unit of GE Healthcare with 425 employees and the Apotek Produktion & Laboratorier unit with about 95 employees, both located in Umeå. AstraZeneca has closed its unit. A company which has grown is Swetree Technologies which had 17 employees in 2012.



In the Örebro County there are 10 companies with 744 employees. Most are manufacturing units and include Cambrex Karlskoga (almost 300 employees), Nobel Biocare and Recipharm Karlskoga as the largest. The employment has grown by about 300 since 1998 but it has been almost constant the last five years.

10 Discussion

Swedish actors have had a long tradition of successfully bringing radical life science innovations to world-wide markets. Flat, non-hierarchical organisations, excellent research, an innovation-friendly healthcare system and traditions of multi-disciplinary collaboration between different sectors in society have generated a creative climate for the iterative, evolutionary life science innovation processes. In simple terms, one part of the present Swedish life science industry encompasses a group of profitable, mature companies stemming from innovations arising during the 1940s to the 1980s. These mature companies have world-wide presence and often high shares of global markets for high-end products with proven quality and worth. At the other end of the industry there is a multitude of recently started companies stemming from innovative research and innovation milieus linked to academia. These have yet to become fully-fledged. In the middle there are about 50 companies with 50-250 employees, with R&D and/or manufacturing in Sweden. Many of these have grown, particularly in the beginning of the time-period studied.

The image of the mature companies (often with a foreign parent company) maintaining their presence in Sweden has, in recent years, been challenged by a number of decisions to close Swedish operations. The examples include both manufacturing and R&D units. At the same time, most of foreign-owned companies are keeping a Swedish presence through investing in Swedish operations and some are also increasing the presence they already have. In order for a continued positive trend, the Swedish presence needs to be seen as continuously contributing to the companies' innovation processes and competitiveness, drawing on a collaborative climate in an eco-system of relevant actors such as suppliers, academia and the health service, as well as an international network. To be an attractive milieu for collaboration, excellence in science and incentives for clinicians to do research and collaborate with industry is needed. These companies have a global presence and there are several alternatives regarding where their R&D is to be located. Thus there is a real risk that they find more competitive milieus in other countries, which also represent larger markets.

Depending on the market, sometimes companies need to "reinvent" their products. Companies may have to change the products for specific markets owing to issues such as what is reimbursed, the accepted price level, demands concerning quality, documentation, properties and the associated services, as well as the organisation and working process in the health service in specific countries. This may lead to a need for an R&D presence or R&D collaboration in important markets, to link the innovation processes to the needs of future markets. In particular, public measures to support such collaboration may be fruitful in helping SMEs with limited resources to reach out on global markets. For some countries, an R&D or manufacturing presence is also a prerequisite for market access.

Companies aim to collaborate with key opinion leaders in academia and clinical practice. At the same time, the striving for evidence-based innovations results in a legitimacy among professionals and aids market entry and continued market access. Clinicians active in research

gain insight into the scientific forefront of their field and the outcomes of the latest therapies. This is likely to lead to a more evidence-based medical practice. The discussions on incentives for clinicians to perform clinical research and to collaborate with industry in the innovation processes continue in a number of forums; a recent contribution in Sweden is the government's commission: 'National Coordination of Clinical Studies'[75].

Medical technology is developed in collaboration with the healthcare system in an iterative process. Thus, the healthcare system not only needs to be an active customer, making its needs clear to the industry, it also needs to be an active partner in the development process for innovations to enter the market. This applies throughout the total product life cycle, for instance also to monitor the outcomes of alternative treatments. This raises a number of issues that need to be resolved. Issues such as the prerequisites for such collaboration, public procurement and ethical concerns are often matters of public debate and the focus of policy discussions.

The different business segments and sub-niches of medical technology are becoming increasingly dominated by a few multinational corporations forming oligopolistic markets. Consolidation is ongoing and the small, innovative companies are increasingly tending to become intermediaries licensing inventions to the large corporations, being partners in their innovation process or being acquired when they are successful. Some of the large global corporations have an R&D or manufacturing presence in Sweden, while others have units for marketing, sales and product-related services but may still collaborate with Swedish academia and healthcare sector. This presence can be an entry point to the large corporations for instance for the small, innovative companies but also for collaborative projects with academia and the healthcare system or for attracting inward investments, even if it is unlikely that green field R&D units will be located to Sweden.

For the small, innovative medical technology companies, often academic spin-offs, the challenges in the process of bringing inventions to the market are severe. These challenges include:

- increasing regulatory demands,
- the need for health economics documentation
- cost containment procedures in the health services
- oligopolies already having large market shares,
- obtaining the resources, knowledge and network needed to reach out to global markets and get the products reimbursed.

Questions thus arise as to how measures to support the SMEs should be designed and which companies should be targeted.

The low R&D productivity of the pharmaceutical industry has led to a focus on reducing the risks, costs and development time in the innovation process. This has led to small firms, large companies and investors all having an increased focus on the use of already evaluated, used, active substances for new indications and in other formulations and combinatory drugs. There is

[75] http://www.regeringen.se/sb/d/108/a/219905

also an increased pipeline in orphan drugs. In these fields, there have been a few examples of very small Swedish companies successfully bringing drug candidates to the market or to a profitable exit. At the same time, new tools are being developed to aid the evaluation of new targets, as well as the identification and validation of candidate drugs. Fragment-based drug design, new therapies such as messenger RNA therapeutics or using RNA molecules to inhibit gene expression (RNA interference) and other scientific breakthroughs are gaining interest. In the stem cell area, induced pluripotent stem cells have been in focus and several Big Pharma companies are involved in exploratory research in regenerative medicine. Increasingly, companion diagnostics with the use of biomarkers and genetic diagnostics is being utilised as a way to reach the appropriate patient population. This reduces the risks associated with the regulatory process and positively affects later market access. However, reducing the patient population means that the price per treated patient needs to be increased in order to reimburse the development costs. Questions may arise as to whether the target of public measures should be radical or incremental innovation and what development phase should be in focus in order to spur innovation and growth in Sweden.

Concerning the pharmaceutical regulatory process it is claimed that the costs continue to increase and R&D productivity is decreasing. The advantages of the regulatory process concerning orphan designation has led to many drug discovery companies going in that direction and perhaps even more so than was intended. There is an ongoing debate as to how the approval process can become more effective, for instance through adaptive licensing.

The radical restructuring of Big Pharma companies has led to a drastic downsizing of their in-house R&D. They intend to increasingly rely on external partnering and acquisitions. This has led to a number of countries launching initiatives and changing organisational structures on the system level to make their life science innovation system more attractive for future investments. For instance, the examples from Great Britain are manifold, with systemic changes in the healthcare system, the patent box, SME programmes, investments in strategic areas and new centres of excellence being launched and organised in new ways.

The high-end products of this industry demand huge development costs. To have a chance of market, new products either need to be significantly better than what is already available or compete on price. Health services facing increased healthcare costs judge innovations based on health economic assessments. Products better than those already available may also experience delayed market entry following regulatory approval. This may occur due to the implementation of targeted cost containment processes.

There has previously been a trend in several business segments of increasing manufacturing in Sweden, which even includes repatriation. Recent announcements now show a few examples of a shift towards offshoring certain manufacturing again. Still, some medical technology companies chose to outsource components manufacturing and keep assembly in Sweden. In pharmaceuticals there is still an increasing trend of manufacturing in Sweden, with the exception of one significant biotech production unit being closed which has led to a decrease in that segment.

A tougher life sciences labour market (due to the down-turn in total employment) may lead to difficulties finding employment commensurate with education and experience. This may alter individuals' attitudes towards careers in the life science industry. At the same time, the connections to frontline research, product development and services that improve people's health and wellbeing are factors which will continue to contribute to the attractiveness of the industry.

The increased ICT content is evident in all segments of the life science industry. This includes the analysis of big data, for instance handling and making better use of clinical and biotechnological data in tools for medical and bioinformatics. It also includes many of the medical device companies becoming ICT companies, delivering complex systems integrated with other devices, complex visualisations, and medical informatics solutions, as well as creating interfaces to communicate with ICT tools concerning electronic health records. Recent trends are also for ICT-intensive products and services aimed at end consumers in the area of personal health-related products, with the advantage of not having to go through the procurement processes of the health service.

The structure of the global life science industry is changing, as are the innovation processes and markets. In Sweden, the dominance of the former Astra and Pharmacia and their successors is still apparent, but diminishing. A few of the mature medical technology companies, who are part of large global corporations and have little anchoring in the Swedish innovation system (i.e. few recent incremental or radical innovations of Swedish origin), have left Sweden. The question arises as to how the remaining prosperous companies can become more closely anchored to the Swedish research and innovation milieus in order to secure their continued presence in Sweden.

When it comes to the decrease in the number of micro- and small-sized companies after a long period of growth, there are many plausible explanations. It is difficult to finance the phases until commercial actors such as venture capital or resource-rich partners start contributing to the financing of new ventures. Companies have also sometimes been founded before enough technical or business verification of the idea, and many have ceased employing in the latest five-year period. Another explanation is that more projects are run virtually, using outsourcing and networking in the innovation process, before starting a company. The design of public support of new ventures thus becomes important, so as not to incentivise the too-early forming of companies. There have also been a number of mergers and acquisitions in the Swedish life science industry reducing the number of micro- and small-sized companies.

The analysis also includes the identification of vital business segments which are growing in Sweden and successful on international markets. Areas such as ICT tools, medical devices such as those in radiology and radiation therapy, intensive care and dialysis as well as implants and diagnostics are examples of growing segments. Some of these include companies that need a continued anchoring in attractive research and innovation milieus to prosper and grow or even stay in Sweden.

The global and Swedish restructuring of the industry described above and other changes in the innovation system and innovation processes has led to a stiff challenge for the public part of the

innovation system. This part aims to provide the system with appropriate incentives, support and financing to benefit a prosperous development of old and new ventures. Changing conditions in global innovation processes raise several discussion points whose answers must be constantly adapted. These include: how improved anchoring of mature companies can be achieved, how the development of attractive research and innovation milieus can be supported, how actors in the system can accumulate the knowledge needed to provide professional advice to those embarking on new ventures, how the selection of what ventures to support should be designed as well as what knowledge is needed as input to the design of support and the selection of projects.

The present analysis provokes new hypotheses and raises follow-on questions. Examples include:

- What happens in the companies which become foreign-owned?
- What are the effects of cultural differences after a foreign take-over; how does the take-over change the innovation processes, productivity and anchoring in Sweden?
- Do the large companies find the competencies and network they think they need in Sweden?
- What role does the Swedish unit gain in a large corporation after an acquisition?
- What happened with the original idea of ceasing ventures? Why did the idea not stick (i.e. what went wrong) and what success factors are there in other ventures?

Appendix

List of companies Sweden

Companies with activities in research and development, consultancy and manufacturing are below listed according to size and business segment. Companies focusing on sales and marketing of life science products are listed at the end and distributed into Pharmaceuticals, Medical technology and Biotechnology. Only companies with their core competence and majority focus in the included business segments and with employees in 2012 are included in the listing and in the analysis of the present report. The listing is found on the VINNOVA website as a separate file.

Tables

Number of employees in the included business segments years 1998-2012 (excluding sales and marketing)

Business segment	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Drug discovery, development, delivery and production	16 023	15 622	16 036	16 127	18 618	17 757	17 478	16 460	17 022	15 907	14 606	13 987	13 503	12 900	12 399
In vitro diagnostics	420	432	442	606	696	722	1 309	1 250	1 210	1 220	1 216	1 230	1 243	1 226	1 278
Biotech medical technology	265	313	372	494	625	555	671	713	734	816	855	805	765	775	781
CRO	358	431	515	696	757	722	700	770	851	974	1 046	1 057	1 041	1 078	859
Biotech tools and supplies	1 293	1 544	1 820	2 104	2 300	2 298	2 142	2 353	2 358	2 423	2 345	2 217	2 266	2 267	2 256
Biotech production	999	995	1 018	1 056	1 133	1 161	1 173	1 140	1 163	1 167	1 224	1 061	944	901	822
Agro-, environmental and food related biotechnology	750	785	835	785	723	724	736	729	730	675	659	675	678	634	542
Healthcare facility products and single-use products	2 430	3 168	3 096	3 097	3 229	3 345	3 488	3 443	3 521	3 364	3 415	3 390	3 375	3 393	3 187
Implantable devices - active and non-active	1 096	1 103	1 537	1 781	2 004	2 211	2 208	2 311	2 425	2 581	2 525	2 570	2 592	2 644	2 493
Anaesthetic and respiratory devices	1 176	1 563	1 561	1 464	1 517	1 414	714	636	560	568	615	594	617	602	623
Electromechanical medical devices	1 019	1 149	1 228	1 329	1 378	1 338	1 346	1 369	1 488	1 584	1 612	1 587	1 520	1 573	1 712
Radiation and imaging devices	434	444	563	729	867	944	988	1 009	1 035	1 077	1 127	1 123	1 044	1 008	1 035
Information and communication tools	124	137	184	255	297	328	329	383	476	539	551	571	626	674	793
Assistive products for persons with disability	545	583	679	687	734	748	781	801	854	923	921	909	907	883	872
Total	26 932	28 269	29 886	31 210	34 878	34 267	34 063	33 367	34 427	33 818	32 717	31 776	31 121	30 558	29 652

Number of companies in the included business segments years 1998-2012 (excluding sales and marketing)

Business segment	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Drug discovery, development, delivery and production	63	77	83	100	108	110	125	128	139	149	150	157	157	153	146
In vitro diagnostics	29	27	31	38	36	37	39	39	46	45	47	43	42	42	37
Biotech medical technology	18	20	19	22	25	25	28	29	30	31	34	31	30	29	30
CRO	39	46	51	56	61	67	72	76	83	95	103	100	102	100	94
Biotech tools and supplies	26	36	48	57	60	63	67	70	77	79	78	81	82	77	74
Biotech production	22	23	24	24	25	27	28	29	31	30	32	29	30	28	27
Agro-, environmental and food related biotechnology	19	23	26	28	29	31	33	34	33	32	33	31	33	33	34
Healthcare facility products and single-use products	90	97	98	106	109	108	114	114	118	115	120	120	114	110	110
Implantable devices - active and non-active	24	25	30	32	33	36	35	34	32	37	38	40	39	40	39
Anaesthetic and respiratory devices	10	14	15	18	17	16	18	17	15	15	13	13	13	12	12
Electromechanical medical devices	31	33	38	40	44	46	52	56	60	62	61	58	54	54	54
Radiation and imaging devices	20	21	25	28	28	31	37	39	40	41	41	38	38	37	33
Information and communication tools	19	21	24	31	34	40	47	51	55	60	61	63	66	62	64
Assistive products for persons with disability	37	38	46	46	50	51	50	52	50	53	49	47	43	40	37
Total	447	501	558	626	659	688	745	768	809	844	860	851	843	817	791

Regional distribution of the number of employees and number of facilities 2012

	Number of employees	Share of employees [%]	No. establishments	Share of establishments [%]
Stockholm	9 999	33,72	536	35,6
Uppsala	4 541	15,31	181	12,0
Södermanland	396	1,34	12	0,8
Östergötland	687	2,32	52	3,5
Jönköping	444	1,50	15	1,0
Kronoberg	357	1,20	8	0,5
Kalmar	31	0,10	4	0,3
Gotland	5	0,02	1	0,1
Blekinge	16	0,05	6	0,4
Skåne	4 835	16,31	317	21,1
Halland	718	2,42	32	2,1
Västra Götaland	5 349	18,04	213	14,2
Värmland	53	0,18	9	0,6
Örebro	744	2,51	12	0,8
Västmanland	76	0,26	10	0,7
Dalarna	193	0,65	10	0,7
Gävleborg	5	0,02	3	0,2
Västernorrland	378	1,27	15	1,0
Jämtland	15	0,05	3	0,2
Västerbotten	654	2,21	56	3,7
Norrbotten	159	0,54	10	0,7
Sweden	29 652	100	1 505	100

Participation in the EU Seventh Framework Programme

	FP7 No. Participations	ENERGY	ENVIRONMENT	European Research Council	HEALTH	ICT	KBBE, Food, Agriculture and Fisheries, and Biotechnology	NMP	PEOPLE	SECURITY	Science in Society	Research for the benifit of SMEs
AstraZeneca	14				4	2		1	7			
Cellectis	8				7				1			
Olink	6				5				1			
Nanologica	6				1			3	2			
Tataa Biocenter	6				2	2			2			
Gems Pet Systems	5					1		1	2		1	
Beactica	5				4				1			
Kdev Exploratory	4				3				1			
Swetree Technologies	4						3	1				
Q-Linea	4				2		1			1		
Agilent Technologies Sweden	3				3							
Mip Technologies	3							1	2			
Newron Sweden	3				1			1	1			
Biotech Invest i Albano	3	1						1	1			
Bactiguard	2				1							1
Novavax	2				1		1					
Avaris	2				1				1			
Protista Biotechnology	2								2			
Redoxis	2				2							
Yh Youhealth	2				2							
Acureomics	2				1				1			
Axcentua Pharmaceuticals	2				1				1			
Sigolis	2				2							
Vironova (Publ)	2				2							
Evitraproteoma	2								2			
Quickcool	2				2							
Multid Analyses	2					2						
Swedish Oat Fiber	2						2					
Fujirebio Diagnostics	2				1	1						
Absorber	1				1							
Alligator Bioscience	1								1			
Anamar	1							1				
Anoxkaldnes	1		1									
Q-SENSE AKTIEBOLAG	1							1				
Gmf Fastighets	1								1			
Diamyd Medical	1				1							
Elekta (Publ)	1				1							
Elos Medtech Microplast	1							1				
GE Healthcare Bio-Sciences	1				1							
Immun System I.M.S.	1				1							

	FP7 No. Participations	ENERGY	ENVIRONMENT	European Research Council	HEALTH	ICT	KBBE, Food, Agriculture and Fisheries, and Biotechnology	NMP	PEOPLE	SECURITY	Science in Society	Research for the benifit of SMEs
Hotswap Stockholm	1				1							
Inovacia	1				1							
Athera Biotechnologies	1				1							
LAYERLAB AKTIEBOLAG	1							1				
Medivir	1				1							
Permobil	1					1						
Raysearch Laboratories (Publ)	1				1							
Saromics Biostructures	1											1
St. Jude Medical	1							1				
Swedish Orphan Biovitrum (Pub	1				1							
Binary Bio	1			1								
Viscogel	1											1
Ot Chemistry	1				1							
Xbrane Bioscience	1				1							
Qlucore	1				1							
Lavivo	1											1
Cavidi	1				1							
Hvre Intressenter i Stockholm i	1							1				
Denator	1				1							
Novosense	1							1				
3H Biomedical	1				1							
Neodynamics	1				1							
Pharma Consulting Group In Up|	1											1
Clinical Gene Networks	1				1							
Scanbi Diagnostics	1											1
Premacure	1				1							
Ortoma	1							1				
Bio-Hyos	1							1				
Scandinavian CRO	1				1							
Genovis	1				1							
Omnitor	1					1						
Bioinvent International	1				1							
Bohus Biotech	1											1
Stricent	1											1
Gotovax	1											1
Nordforce Technology	1					1						
Isosep	1								1			
Corline Systems	1											1
Mabtech	1				1							
Total	**154**	**1**	**1**	**1**	**72**	**11**	**7**	**18**	**31**	**1**	**1**	**10**

Interviews

To gain insights beyond the statistical data and literature, comments regarding life science trends have been gathered through interviews for all previous VINNOVA life science studies as well as this one. Within the process of compiling the present analysis, the following people have been interviewed or have commented on drafts of the report.

Anders Blanck, LIF

Anders Weilandt, Diabetes tools

Anna Cherouvrier-Hansson, Invest in Skåne

Bertil Guve, Center for Technology in Medicine and Health

Björn Walse, Saromics Biostructures

Bo Norrman, Chalmers

Heather Marshall-Heyman, KaroBio

Håkan Larsson, previously AstraZeneca (Mölndal)

Jonas Ekstrand, SwedenBIO

Johan Mälsjö, Siemens

Johan Drott, Respiratorius

Johan Thorwid, Cambio Healthcare

Lars Åke Malmsten, Lidds

Lena Blom, Siemens

Ola Björkman, Stockholm Uppsala Life Science

Peter Bramberg, Business Sweden

Petrus Laestadius Swedish Medtech

Pontus Ottosson, Puls Invest

Sören Johansson, Elekta

Ursula Hultkvist Bengtsson, Medicon Village (previously AstraZeneca Lund)

Sources

This study was based on the database built up within the framework of past VINNOVA reports in this field (VA 2003:2, VA 2005:2,VA 2007:16, VA 2008:10, VA 2011:03 and VA 2012:07), regional input and input from university holding companies, Almi AB, Trade Associations,Venture Capital firms plus VINNOVA, and the EU in regard to companies having received funding.

The data was supplemented by drawing on data lists for companies with NACE codes 21100, 21200, 26600, 32501, 32502, 46460, 47730, 47740, 71129, 71200, 72110 and 72190. Concerning companies identified by a NACE code, only those with at least one employee were categorised. In total, approximately 4 000 companies were categorised within the framework of this study. Companies were categorised on the basis of information from the companies' websites, other information on the Internet, patent applications, various studies and analyses on companies within the field and telephone conversations with many of the companies. Information about the number of employees of each company, the year of establishment, the structure of groups of companies as well as the economic information was extracted from Soliditet AB and PAR AB. Their databases are based on information registered at the Swedish Companies Registration Office.

OECD biotechnology definition

The application of science and technology to living organisms as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services

OECD list-based definition of biotechnology techniques

DNA/RNA: Genomics, pharmacogenomics, gene probes, genetic engineering, DNA/RNA sequencing/synthesis/amplification, gene expression profiling, and use of antisense technology.

Proteins and other molecules: Sequencing/synthesis/engineering of proteins and peptides (including large molecule hormones); improved delivery methods for large molecule drugs; proteomics, protein isolation and purification, signalling, identification of cell receptors.

Cell and tissue culture and engineering: Cell/tissue culture, tissue engineering (including tissue scaffolds and biomedical engineering), cellular fusion, vaccine/immune stimulants, embryo manipulation.

Process biotechnology techniques: Fermentation using bioreactors, bioprocessing, bioleaching, biopulping, biobleaching, biodesulphurisation, bioremediation, biofiltration and phytoremediation.

Gene and RNA vectors: Gene therapy, viral vectors.

Bioinformatics: Construction of databases on genomes, protein sequences; modelling complex biological processes including systems biology.

Nanobiotechnology: Applies the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics etc.

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VINNOVA Analysis
VA 2014:

01 Resultat från 18 VINN Excellence Center redovisade 2012 - *Sammanställning av enkätresultaten. For English version see VA 2014:02. Only available as PDF*

02 Results from 18 VINN Excellence Centres reported in 2012 - *Compilation of the survey results. For Swedish version see VA 2014:01. Only available as PDF*

03 Global trends with local effects - *The Swedish Life Science Industry 1998-2012*

VA 2013:

01 Chemical Industry Companies in Sweden

02 Metallindustrin i Sverige 2007 - 2011

03 Eco-innovative Measures in large Swedish Companies - *An inventory based on company reports*

04 Gamla möjligheter - *Tillväxten på den globala marknaden för hälso- och sjukvård till äldre*

05 Rörliga och kopplade - *Mobila produktionssystem integreras*

06 Företag inom miljötekniksektorn 2007-2011

07 Företag inom informations- och kommunikationsteknik i Sverige 2007 - 2011

08 Snabbare Cash - *Effektiv kontanthantering är en tillväxtmarknad*

09 Den svenska maritima näringen - *2007 - 2011*

10 Long Term Industrial Impacts of the Swedish Competence Centres

11 Summary - Long Term Industrial Impacts of the Swedish Competence Centres. *Brief version of VA 2013:10*

12 Företag inom svensk gruv- och mineralindustri 2007-2011

13 Innovationer och ny teknik - *Vilken roll spelar forskningen*

14 Företag i energibranschen i Sverige - *2007-2011*

15 Sveriges deltagande i sjunde ramprogrammet för forskning och teknisk utveckling (FP7) - *Lägesrapport 2007-2012. Only available as PDF*

16 FP7 and Horizon 2020. *Only available as PDF*

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01 Impact of innovation policy - *Lessons from VINNOVA´s impact studies. For Swedish version see VA 2011:10*

02 Lösningar på lager - *Energilagringstekniken och framtidens hållbara energiförsörjning*

03 Friska system - *eHälsa som lösning på hälso- och sjukvårdens utmaningar*

04 Utan nät - *Batterimarknadens utvecklingsmöjligheter och framtida tillväxt*

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09 Uppföljning avseende svenskt deltagande i Eurostars. *For English version see VA 2012:10. Only available as PDF*

10 Follow-Up of Swedish Participation in Eurostars. *For Swedish version see VA 2012:09. Only available as PDF*

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VI 2014:

01 Tjänsteinnovationer 2007. *Only available as PDF*

02 Innovationer som gör skillnad - *en tidning om innovationer inom offentliga verksamheter*

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01 Branschforskningsprogrammet för skogs- & träindustrin - *Projektkatalog 2013*

02 Destination Innovation- *Inspiration, fakta och tips från Ungas Innovationskraft*

03 Inspirationskatalog - Trygghetsbostäder för äldre

04 Challenge-Driven Innovation - Societal challenges as a driving *force for increased growth. For Swedish version see VI 2012:16*

05 *Replaced by VI 2013:14*

06 Årsredovisning 2012

07 Trygghetsbostader för äldre - *en kartläggning. Only available as PDF*

08 Äldre entreprenörer med sociala innovationer för äldre - *en pilotstudie kring en inkubatorverksamhet för äldre. Only available as PDF*

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16 *Replaced by VI 2013:22*

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21 OECDs utvärdering av Sveriges innovationspolitik - *En sammanställning av OECDs analys och rekommendationer.*

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03 Idékatalog - Sociala innovationer för äldre

04 *Replaced by VI 2013:05*

05 Årsredovisning 2011

06 *Replaced by VI 2012:15*

07 *Replaced by VI 2013:18*

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03 Utvärdering av Strategiskt stålforskningsprogram för Sverige - *Evaluation of the Swedish National Research Programme for the Steel Industry*

04 Utvärdering av Branschforsknings-program för IT & Telekom - *Evaluation of the Swedish National Research Programme for IT and Telecom*

05 Metautvärdering av svenska branschforskningsprogram - *Meta-evaluation of Swedish Sectoral Research Programme*

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10 Den innovativa vården

11. Framtidens personresor - *Slutrapport. Dokumentation från slutkonferens hösten 2011 för programmet Framtidens personresor*

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