Fraunhofer Institute
Systems and
Innovation Research

Research on the Estonian biotechnology sector innovation system

Final report submitted to Enterprise Estonia, Tallinn

Dr. Klaus Menrad
Dr. Bernhard Bührlen
Dr. Sibylle Gaisser
Dr. Sybille Hinze
Dr. Martina Menrad
Dr. Thomas Reiss
Dr. René Zimmer

Fraunhofer Institute for Systems and Innovation Research
(Fraunhofer ISI)
Breslauer Str. 48
76139 Karlsruhe
Germany

February 2003

List of contents

page

List of tables

page

List of figures

Executive Summary

Introduction and methodology

Modern biotechnology is considered as a key technology of the 21st century. In this sense, biotechnology represents one of the driving forces of the future technological development and is often seen to create the next techno-economic paradigm. Due to its multidisciplinary character, modern biotechnology is pre-destined for creating links between different technological areas (like e. g. micro- or nanotechnology, material sciences, information technologies or specific areas of chemistry). The expected effects of biotechnology will probably develop completely in the medium- to long-term. Due to the long time horizons which have to be taken into account in research-intensive technologies with a fast moving science base, it is necessary to create a fertile platform for the future development of biotechnology already today.

In this context Estonia has started to develop a general framework for scientific research, commercial exploitation of new scientific knowledge as well as industry-related R&D and innovation activities by publishing a national research and development strategy paper in 2001 ("Knowledge-based Estonia") in which biomedicine is defined as one of three technology key areas for future development. As a first step in order to establish a national biotechnology programme, the Ministry of Economic Affairs and Communications of Estonia initiated a study which analysed the Estonian innovation system in biotechnology. This project was carried out by the Fraunhofer Institute for Systems and Innovation Research (Fraunhofer ISI), Karlsruhe (Germany) and financed by Enterprise Estonia.

The study builds on a methodological set, consisting of reviewing existing literature and reports, a questionnaire-based survey among companies, research institutions and service providers as well as face-to-face interviews with 55 actors in Estonia belonging to the same target groups. In order to compare the Estonian situation in biotechnology with other countries, the biotechnology innovation system was analysed in the EU countries Austria, Finland, Germany, UK, and Ireland as well as the USA. In addition to available scientific literature and reports, specific bibliometric, patent and economic indicators were created measuring the performance of the innovation systems. This information was used to benchmark the Estonian situation against those in the other European countries. Finally, the project team of Fraunhofer ISI elaborated preliminary policy recommendations which will be discussed at a stakeholder meeting scheduled for February 25th, 2003 in Tallinn.

Biotechnology innovation system in Estonia

B

The results of the analyses carried out in the frame of the project are presented following a systems approach which encloses the interactions between the different actors and influential factors relevant to innovations in biotechnology in Estonia.

Knowledge/skills network

Currently more than 15 different research institutions with an overall permanent staff of approximately 300 people are directly linked to the field of biotechnology. In the Tallinn region key actors in biotechnology research are the National Institute of Chemical Physics and Biophysics (KBFI), the Tallinn Technical University (TTU), the Estonian Institute of Experimental and Clinical Medicine and the Plant Biotechnology Research Centre (EVIKA). Key actors in biotechnological and medical research in the Tartu region are the Estonian Biocentre (EBC), various institutes of the Tartu University (e. g. Institute of Molecular and Cell Biology) and the University Clinics as well as the Estonian Agricultural University. The Estonian Genome Project represents a unique project compared to other human genome projects world-wide since it is intended to collect genom-, proteom- and health-related data of a high number of healthy people.

Financing of research in Estonia is limited through the fact that only 0.75 % of GDP are spent on research, with 80 % out of this from public sources. In the research institutions related to biotechnology around 35 % of the annual funding originates from basic funding provided by the Estonian Government, nearly 40 % comes from Estonian project funding and around 12 % from EU funds. Other sources (like other governments, industry, clinical trials, counselling) are of minor relevance. The main research financing institutions from Estonia were the Ministry of Education, the Estonian Science Foundation and – for very few institutions – ESTAG. In relation to EU projects, there was a strong discrepancy between the stated relevance of such projects during the interviews and the factual proportion of them in the institutes' budgets.

All interviewed research institutions were able to recruit graduates and postgraduates with relevant biotechnology knowledge and skills. The major problem to get qualified staff is the salary research institutions are able to pay (around 60 % of those paid in industry and public agencies). Most of the interviewed researchers tend to train their technical staff on the job. Often bachelor students are mobilised for technical work in the laboratories as well. The number of students in the life science sector and informatics rose constantly during the last years, but the increased number of undergraduates did not lead to a proportional increase in graduate students so far. In mathematics, natural sciences and engineering disciplines a moderate interest of students can be registered in the last years often resulting in lack of specialists in the related industries. In addition, the organisation and quality of vocational training does not follow the requirements of companies operating in Estonia.

Altogether, the following *strengths* can be observed related to the knowledge base:

- Well-defined internal networks of the main scientific and commercial actors in biotechnology in Estonia which facilitate the realisation of scientific projects and commercial activities.
- Substantial amount of research activities in the biomedical field in Estonia which are strongly interlinked with research groups in other European countries.
- Sufficient availability of qualified staff at least in the core disciplines related to biotechnological research.
- Increasing interest of students in the field of life sciences and informatics.

On the other hand, the following *weaknesses* related to the knowledge base emerged during the analyses:

- Lacking funds for interdisciplinary research.
- Subcritical R&D capacities and activities in application areas of biotechnology outside the biomedical field.
- Availability of scientific infrastructure (like equipment pools and laboratory space), in particular in the Tallinn region and in Tartu outside the biomedical field.
- Low interest of high school students in science and engineering studies.
- The needs of potential user industries of biotechnology (e. g. pharmaceutical, chemical, food industry, wood processing) are not adequately considered in the current academic education of students. The same relates to the integration of biotechnology-related management and business aspects in the scientific education.
- Technical staff often is not educated in modern biotechnological methods and techniques and trained with up-to-date laboratory equipment.

Industry/supply network

In Estonia there are 11 core biotech companies with about 145 employees. If a less stringent definition is used, the number of companies increases to 24 which employ around 160 people. The total turnover of the biotech companies amounts to about 50 million EEK. Most of the companies are active in the biomedical field or related to bioinstruments. In 2002 only five of the biotech companies employed more than 10 people although some of the companies showed an impressive growth in the last years. In spite of their small size most of the companies generate some turnover often by selling standard type biotech-related products or services. In this sense the "business model" of most Estonian biotech companies differs significantly from those in the EU and the USA mainly due to lack of (seed) venture capital and alternative financing possibilities for business activities in high tech fields in Estonia. So far only two Estonian biotech companies (Asper Biotech, EGeen) were able to acquire international venture capital funds.

Due to the small domestic market, most of the Estonian biotech companies are at least partly export-oriented and generate some turnover on EU or the US market. However, several company owners do not follow an explicit business strategy and try to grow rather incrementally in order to minimise their own financial risk. In addition, a clearly defined marketing strategy and experiences of the management in this respect are missing in most Estonian biotech companies. The big majority of the Estonian biotech firms does not apply an active patenting strategy due to lack of knowledge and financial resources and thus does not fulfil important prerequisites for acquiring venture capital. Related to personnel, interviewees mentioned lack of biotech managers as a problem (like in other European countries), but most firms are able to recruit graduates and postgraduates with knowledge and skills in modern biotechnology mainly due to the fact that biotech companies pay higher wages than academic institutions.

In contrast to the already existing commercialisation activities in particular in the biomedical field resulting in a relatively high number of biotech companies in relation to the population in Estonia, the following *weaknesses* are registered in relation to the industry/supply network:

- Lack of or missing availability of technical infrastructure and up-to-date and expensive scientific equipment (e. g. for genome sequencing or proteine analysis, high-standard safety laboratories, high-speed Internet links) both for research activities in the biotechnology field as well as commercialisation activities of scientific findings.
- Public and private services and support in IPR issues and business activities (like general management techniques, marketing, distribution or production management) related to dedicated biotechnology companies.
- Vocational training in modern biotechnology techniques both for scientific and technical personnel.
- Low awareness of personnel development needs in biotechnology companies and traditional user industries.

Finance/industrial development network

Private financing of business activities was outlined as one of the major problems in the biotech field. Currently, the Estonian financial market is characterised by a low amount of venture capital, in particular for the seed and start-up phase of a company, as well only very few venture capital companies being active in Estonia. Mainly due to the high risk and lack of experience, most of these venture companies did not invest in biotech companies so far. Venture companies concentrate their fund-raising activities on private investors, who are extremely short-term oriented what also hinders direct investments of them in biotech companies. In addition, a limited set of (commercial) instruments to business financing poses another constraint for company founding and growth in the biotech field.

Public (co-)financing of innovation activities is provided by ESTAG in form of grants or loans. In 2001 36 % of all financing decisions of ESTAG related to bio- and food technology with a total financial volume of 17 million EEK. The interviewed representatives of biotech companies regarded the application procedure for ESTAG funding as "demanding" but they agreed that it could be realised with the support provided by ESTAG. The evaluation procedure of ESTAG as well as the time requirements for this process were critically commented during the interviews.

In contrast, the general infrastructure and the entrepreneurial climate was perceived as being favourable in Estonia. This relates in particular to the corporate tax system with specific advantages for companies (e. g. to reduce the tax burden if profits or revenues are re-invested in the business), a low level of bureaucracy (e. g. for company registration) and the generally liberal economic policy of the Estonian Government. However, the following *weaknesses* have to be mentioned in the financial/industrial development network as well:

- The very short-term perspective of existing investment schemes and expectations of potential investors do not meet the requirements of biotechnology companies.
- There is almost no investment capital for the seed phase of a biotech company available in Estonia.
- Lack of general instruments for business financing due to the low interest of private banks or other financing institutions.

Market/social acceptability network

The regulation of pharmaceuticals and (bio)medical devices in Estonia is adopted to those of the EU member countries, i. e. the state controls the market approval of pharmaceuticals and registers them with the help of the State Agency of Medicine which is located in Tartu. In Estonia there is a simplified procedure of recognition for medicinal products authorised in the EU by the centralised procedure. Clinical trials are regulated in Estonia according to similar rules like in the EU. The same applies to medical devices, where important EU directives have been implemented by the Medical Devices Act in 2001.

In December 2000 the Estonian Parliament passed the Human Genes Research Act which establishes guidelines for the Estonian Genome Project. Important rules state that the participation in this project is voluntary and that the gene donors' identities are kept confidential. For this purpose their personal data have to be separated from genetic data. In addition, the gene donor has the right to know or not to know his/her genetic data and nobody should be discriminated due to his/her genetic information.

Related to genetically modified organisms Estonia has adapted its regulations to those of the EU in the last years and transferred all relevant EU directives into Estonian law. Three ministries (Environment, Agriculture and Social Affairs) are responsible for the implementation of the different EU regulations in Estonia assisted by two advisory bodies (Advisory Committee for Genetic Modification, Novel Food Advisory Committee) which discuss applications for market approval of GMOs as well. Altogether the analyses revealed the following *strengths* of the innovation system in this field:

- Adequate legal framework in the medical field and related to genetically modified organisms.
- With the Human Genes Research Act Estonia has established one of the first regulations in the field of human genetics world-wide and created a stable legal framework in this area.
- User-friendly implementation and application of the specific regulations related to biotechnology.
- Neutral to positive attitude of the population in relation to biotechnology research and application.

Modern biotechnology tools and techniques can be used in a variety of traditional industries which are relevant for the overall economy in Estonia as well. This relates in particular to the chemical industry (with around 4,600 employees in 2000, 6.6 % of the total production of the manufacturing industry), the food processing industry (with 14,800 employees in 2001, around one quarter of industrial production) and the wood-processing industry with more than 15 % of total industrial output of Estonia. In contrast, a R&D-oriented pharmaceutical industry as well as biomedical companies are almost totally lacking in Estonia. With respect to the market/social acceptability network the following *weaknesses* emerged during the analyses:

- In most biotechnology companies there is a low awareness and lack of experience related to marketing needs as well as management options in this area.
- Lack of awareness of potential traditional user industries (e. g. food, chemical and wood-processing industry) of the benefits and potentials of innovative technologies in general and modern biotechnology in particular.
- Absence of Estonian R&D-oriented pharmaceutical companies impedes the domestic commercialisation of scientific findings in the biomedical field.
- Small domestic market in Estonia and in consequence the need to access international markets also for young and small-sized companies which often

lack specific knowledge on the situation and development of international markets as well as marketing and adequate business strategies.

Altogether, a relatively limited impact of biotechnology on the overall Estonian economy in terms of employment, production and exports can be expected in the coming years without specific initiatives of the Estonian Government. The major challenges for the future development of the biotechnology innovation system in Estonia relate to substantiate the research activities in the biomedical field, to build up the management and marketing skills of the company founders and managers in this area, to develop the research activities in the non-medical fields of biotechnology, to awake the interest of the traditional industries in innovation and modern technologies in general and biotechnology in particular, to improve the co-operative climate between biotechnology-related disciplines and locations within Estonia, as well as to further develop the financial instruments and the capital market for high-tech industries in Estonia. Furthermore, it should not be assumed that the attractiveness of Estonia as a biotech location will significantly increase just due to the EU access of this country.

Benchmarking of the Estonian innovation system with reference countries

The qualitative benchmarking of the Estonian *knowledge/skills network* reveals that the difficulties to establish an interdisciplinary organisation of biotechnology-related research in Estonia are similar to those in most reference countries. However, in some of these countries specific funding initiatives have already been taken to tackle this problem. Concerning the application of biotechnology in other research areas such as chemical research or food and nutrition-related research Estonia seems to be less advanced than most of the reference countries. In contrast the integration of biotechnology into the biomedical field is well established and comparable with the reference countries.

Modern biotechnology research increasingly relies on the availability of large scale and expensive equipment, so that the accessibility of such equipment for interested users is an important success factor. In Estonia we found pronounced regional and sectoral differences related to this issue in a sense that the availability of up-to-date scientific infrastructure is a particular problem in the Tallinn region and in the Tartu area mainly outside the biomedical field. Setting up centres providing such infrastructure has been a common strategy in several countries to improve this situation.

Biotechnology with its strong knowledge intensity requires highly qualified and skilled personnel. Therefore it is important that already at high school level interest in science and engineering can be raised. In Estonia as in many of the reference countries interest in science and engineering seems to cease at high school level. In some countries specific awareness campaigns targeted at schools have been initiated in order to improve the situation. The availability of skilled technical staff becomes increasingly important for biotechnology not least due to the growing "technisation and automatisation" of this sector. Though this is a problem in particular in those countries where the biotech industries are well developed. Estonia already today is facing problems in this field. It seems that vocational training in general has a low image in Estonia compared with the international situation. Another problem in Estonia concerns the match between higher education and the needs of industry which seems to be less developed than in the reference countries. This might be due to the fact that in these countries various measures have been taken in order to improve the adjustment of academic education to industrial needs.

The international comparison of the Estonian *industry/supply network* firstly reveals an unfavourable situation in this country with respect to the access for companies to technical infrastructure and modern and expensive equipment. In addition, lacking market and business orientation of biotechnology companies seems to be a more serious problem in Estonia than in the reference countries. In most of these countries since some time specific measures have been taken to provide the required business information and support for new biotechnology firms. Biotechnology bears the potential to improve the economic situation of a number of traditional user industries. Presently these indirect effects of biotechnology can be observed mainly in the pharmaceutical sector. It is expected that the chemical and the food sector will follow this example in the near future. Comparing Estonia with the reference countries reveals that the required links between such user industries and biotechnology are less developed, which might be due to the fact that since a couple of years specific measures have been taken in these countries aiming at improving the adoption of biotechnology by user industries.

The international benchmarking of the *finance/industrial development network* for biotechnology indicates that the general entrepreneurial climate in Estonia compares favourably with the reference countries. However, as a general problem the short-term perspective of current financing schemes and the views of investors in Estonia make the development of medium-term oriented and sustainable business strategies rather difficult if not impossible. In particular lacking seed financing is a draw back in Estonia, while in almost all the reference countries specific schemes for providing seed funds have been established in the last years. Further, common instruments for private business financing are becoming increasingly available for biotechnology endeavours internationally. In Estonia such financing schemes are widely lacking.

Considering the *market/social acceptability network* for biotechnology reveals on the one hand an unfavourable situation in Estonia in terms of existence and attractivity of user markets for biotechnology. In particular a lacking domestic pharmaceutical sector and low or absent interest of established user industries in the chemical and the food sector pose specific problems for Estonian biotechnology that are not existing in the reference countries. On the other hand the regulatory framework for biotechnology in Estonia is not different from the reference countries since all relevant EU guidelines and directives have been transferred to national law. As a particular strength of Estonia the human genes research act should be mentioned which provides a stable legal framework for modern human genetic research. In addition, the implementation of the regulatory framework for biotechnology compares well with the most user-friendly approaches in the reference countries.

In terms of scientific performance Estonia has been behind the reference countries during the 1990s by most measures applied. However, it is remarkable that Estonia is performing best among all these countries in terms of growth of scientific performance. Looking in more detail at the Estonian performance for publishing intensities in biotechnology, the rather low amount of gross expenditure in R&D in Estonia seems to be one of the reasons for the performance pattern.

Looking at commercial performance Estonia is doing well in terms of number of biotechnology firms and venture capital invested in comparison to the reference countries. However, it has to be taken into account that the entire venture capital was invested by one venture capitalist in only two biotech companies. In addition, the relatively weak performance in terms of patenting intensities at the European level seems to indicate that the technological basis of the Estonian biotechnology industry is limited so far and may face some difficulties in an international competition.

Recommendations for policy actions

In order to fully exploit the commercial potential of biotechnology in Estonia a dual approach is recommended aiming at both, to develop biotechnology as an important field in the high-tech sector, namely the biomedical area, and as tool to increase innovativeness of the economicly more relevant low- and medium-tech sectors such as food-processing, wood-processing and the chemical industry. The proposed dual stage master plan of *Biotechnology Implementation into Economy* allows synergistic effects between the biomedical sector, which is already advanced in scientific and technical terms, and the low- and medium-tech industries. This will allow to miss out the initial establishing problems in the latter. Additionally it can be assumed that the two stage strategy allows partly the external financing of otherwise internal costs.

We propose to implement a set of measures over a five-years-period in order to improve the Estonian situation in three areas: knowledge base, education, commercial development.

1. Knowledge Base:

- Set up a specific programme for interdisciplinary research in life sciences by the ESF.
- Provide specific funds for updating scientific infrastructures.
- Set up a programme for supporting the adoption of biotechnology in agro-food and chemical research units including funds for modernising infrastructures.

These measures should be implemented as soon as possible because they create the required preconditions for commercial development. The total costs of this part of the programme are estimated to 99 million EEK for five years. About 48 % are planned for interdisciplinary research, 24 % for updating scientific infrastructure, and 28 % for the biotechnology adoption measure.

2. Education

- Establish business education centres at universities.
- Set up an education programme providing grants for international scholarships.
- Introduce industrial internships into master programmes.
- Develop and implement a modern curriculum for education of technicians.
- In addition, interest of high school students for science and engineering should be improved by e. g. initiating awareness campaigns at schools.

Since modifications of educational systems take rather long it is recommended to start the education initiative soon while the business education centre initiative could start about one year after commencement of the total programme. Total costs for the education sub-programme are estimated to about 8.5 million EEK for five years. 44 % would be devoted to business centres (two centres, one in Tartu and Tallinn each), 54 % to financing scholarships (five per year) and 2 % to developing and implementing the technicians curricula.

3. Commercial development

- Establish two science parks related to life science activities, one in Tartu and one in Tallinn.
- Build up information programmes on marketing and business strategies for biotech SME.
- Set up a programme informing traditional industries about biotechnology potentials and providing advice for adoption.
- Set up a procurement initiative for the development of new or improved products based on modern biotechnological methods and tools.

- Set up a seed capital fund for high technology start-ups.
- Initiate a round table for established financing institutions in order to increase awareness for high technology financing.

The commercial initiative should start at the beginning of the programme because it implies a number of planning processes that require a certain period of time. Costs for the commercialisation programme for five years are estimated to about 250 million EEK with the lions share of about 46 % going to the science parks and another 43 % to the seed capital fund. SME information would require about 0.5 %, the adoption programme around 2 %, and the procurement initiative 8.5 %.

On this basis the total costs of the programme are estimated to about 357 million EEK for five years.

The proposed biotechnology strategy for Estonia tackles a broad variety of different individual functions of the innovation system starting from high school education and ending at international marketing of Estonia. This strategy can only be successful if the various initiatives are implemented in a co-ordinated way. In other words, success requires a balanced policy mix, focusing just on individual measures without taking care of their systemic context will most likely result in sub-optimum outcomes.

1. Introduction and targets of the project

Modern biotechnology[1] is considered as one of the key technologies of the 21st century. In this sense, biotechnology represents one of the driving forces of the future technological development and is often seen to create the next techno-economic paradigm. In this context it is expected that biotechnology will contribute to develop new products or services as well as to replace or partly substitute conventional production processes. Currently, modern biotechnology represents already one of the most important tools in the search and development of new active substances in pharmaceutical research (Gambardella et al. 2000, Jungmittag et al. 2000). The same relates to other areas of economy in which searching for specific active substances plays an important role (as e. g. in agro-chemicals or veterinary medicine) (PEW 2001, Dunwell 1999). In all these application areas modern biotechnology provides platform technologies which will become even more relevant in the future (Sager 2001, Menrad et al. 1999). In particular in the pharmaceutical sector it is estimated that no new pharmaceuticals will be introduced to the market that were not influenced by biotechnical research and development (R&D) tools in the coming years. In the second half of the 1990s, 41 % of the world-wide patent applications in the pharmaceutical sector were connected to modern biotechnology, compared to 32 % at the beginning of this decade (Hinze et al. 2001). In the year 2000, 6 % of the global sales of pharmaceuticals were related to biopharmaceuticals and the relevance of this product group is expected to grow significantly in the coming years (VFA 2002, Hinze et al. 2001). In the agricultural field an increasing number of genetically modified plant varieties are commercially available which have been grown on more than 52 million hectares in 2001 mainly in North and South America (James 2001).

An important outcome of modern innovation research states that specific technologies cannot be broken down into individual development lines at the beginning of the 21st century (Grupp 1995), since the different lines of technical development will work together in future. It is assumed that modern biotechnological approaches and tools will play a specific role in this technology network. Due to its multidisciplinary character, modern biotechnology is pre-destined for creating links between different technological areas. The beginning of this multidisciplinary integration process can already be observed in the integration of modern biotechnological tools and approaches in areas such as micro- or nanotechnology, material sciences, information technologies or specific areas of chemistry. The expected effects of biotechnology will probably develop completely in the medium- to long-term. Due to the long time horizons which have to be taken

---

1 Modern biotechnology is understood as "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 2001a).

into account in research-intensive technologies with a fast moving science base (as it is typical for biotechnology), it is necessary to create a fertile platform for the future development of biotechnology already today. This relates e. g. to the science base, entrepreneurial activities as well as to an economic and regulatory framework which supports innovations in biotechnology.

In this context Estonia has started to develop a general framework for scientific research, commercial exploitation of new scientific knowledge as well as industry-related R&D and innovation activities by publishing a national research and development strategy paper in 2001 ("Knowledge-based Estonia") in which biomedicine is defined as one of three technology key areas for future development. In addition, it is foreseen that public and in particular private investments in R&D and innovation activities will be substantially increased until 2006 (Secretariat of the Research and Development Council 2002). Based on this general strategy, it is intended to establish a biotechnology programme in Estonia in the coming year. As a first step in this direction, the Ministry of Economic Affairs and Communications of Estonia initiated a study which analyses the national innovation system in biotechnology in this country. This project is carried out by the Fraunhofer Institute for Systems and Innovation Research (Fraunhofer ISI), Karlsruhe (Germany) and financed by Enterprise Estonia. This final report informs about the results of the analyses and gives recommendations for the further development of biotechnology in Estonia.

The overall target of the project is to analyse the biotechnology innovation system in Estonia in order to prepare the ground for necessary policy actions. The study has the following specific targets:

- Analysis of the biotechnology industry and markets in Estonia and internationally
- Mapping and analysis of the biotechnology knowledge base in Estonia
- Analysis of the framework conditions for biotechnology in Estonia
- Analysis of the potential of biotechnology in key application areas
- Development of recommendations for policy actions

2. Biotechnology innovation system in Estonia

The subsequent analysis of the Estonian biotechnology innovation system follows the concept of the study and uses a systems approach which encloses the interaction between the different actors and influential factors relevant to innovations in biotechnology (for details concerning the methodology and the realised working steps see annex A1). The collection of data was finalised at the beginning of December 2002, so that this report represents the situation at the end of the year 2002. In the following the networks of knowledge and skills, industry and supply, financing and industrial development as well as demand and social acceptability of biotechnology in Estonia are characterised in the subsequent chapters.

2.1 Knowledge/skills network

The chapter knowledge/skills network characterises the key actors in Estonian research institutions according to structures and activities related to biotechnology, research funding possibilities and framework conditions for research. Additionally, vocational and higher education are analysed and the accordance of training facilities and demand are assessed.

2.1.1 Structures and activities of research institutions related to biotechnology

Estonia consists of a vast number of institutions with focus on research in the life science sector. Estonian science has undergone a profound change as a result of independence from Soviet Union in 1991. Of major importance were the take out of research institutes from the Academy of Sciences to operate independently under the general oversight of the Ministry of Education and the removal of the sharp boundaries between research institutes and institutions of higher education. Both actions are assumed by internal and external experts to have been a strong stimulus for the Estonian research (Martinson 1995, Bikales 1996, Tartes 1999).

Today more than 15 different research institutions with an overall permanent staff of approximately 300 people are directly linked to the field of biotechnology. As many institutions are closely linked to each other, this results in a complex structure of the scientific community. In the following the key institutes according to scientific quality and/or sectoral importance for the various dimensions of biotechnology are characterised by their research topics and structure.

In **Tallinn region** key actors in biotechnology research are the National Institute of Chemical Physics and Biophysics (KBFI), the Tallinn Technical University (TTU), the Estonian Institute of Experimental and Clinical Medicine and the Plant Biotechnology Research Centre (EVIKA).

National Institute of Chemical Physics and Biophysics (KBFI)

The National Institute of Chemical Physics and Biophysics (KBFI[2]) was founded in 1980. In 1984 the biotechnological focus was introduced into the research activities by the foundation of the Laboratory of Molecular Genetics (LGM). Currently, KBFI consists of four laboratories, three of which (molecular plant virology, biochemistry, bioenergetics) are active in biotechnological research. From 1997 KBFI staff started teaching of gene technology at Tallinn Technical University (TTU). For that reason the Centre for Gene Technology at TTU was founded, consisting of gene technology, molecular biology and molecular diagnostics chairs. Research is carried out in joint groups where people engaged in TTU are working together with scientists from KBFI. Currently, 60 research scientists are working in three "biology-related" laboratories at KBFI plus 35 research scientist in the laboratory of chemical physics. The KBFI is now an independent research institute working under its own law. In recent years it belonged to the Estonian Academy of Sciences. It was nominated "Estonian Centre of Excellence in Research" by the Ministry of Education in 2001. Today the Centre consists of seven research groups, among them with relevance for the biotechnological development in Estonia are the functional genomics and proteomics group and the mass spectrometry group as supporting structure.

The KBFI intends to unify different disciplines such as physics, chemistry, engineering and biology under one roof in order to facilitate interdisciplinary research, especially the application of optical methods in biology. This could be a unique selling point of the KBFI which is, however, not exploited sufficiently. To take advantage out of this constellation the strategic planning and focusing of the institutes research policy should be further implemented. The KBFI has research facilities that allow the consecutive research from the single molecule up to the production by fermentation and down-stream processing. However, without connection of these fermentation facilities to the practical testing of fermented products in animal testing and clinical trials either in-house or in co-operation with experienced research institutions the commercial potential of the fermentation facilities cannot be exploited sufficiently. Thus, co-operations with medical institutions for clinical trials should be established. External evaluators assessed the research conditions (infrastructure, outdated equipment) as rather bad and

---

2 We use the Estonian abbreviation also in the English text instead of the English abbreviation NICPB, as we got the impression that this version is more common in Estonia.

concluded that the institute was unable to perform its function under these conditions (Vaheri et al. 2000).

Tallinn Technical University

The Tallinn Technical University has selected eight Centres of Excellence, among them in the life sciences sector are the Centre of Biomedicine and Biotechnology and the Centre of Biomedical Engineering. To promote the relationship between Academia and Industry the University has launched the programme of Centres of Technological Competence. Within the programme activities are the formalisation of collaborative research projects and the creation of business contacts. One out of five Centres of Competence has its research activities in the life science sector: the Centre of Gene- and Biotechnology.

Institute of Food Technology

The Institute of Food Technology at the Tallinn Technical University has focused its research both on classical aspects of biotechnology (e. g. fermentation of food) and of basic research related to the above mentioned aspects (e. g. cell metabolism, modelling of microorganisms). To allow process control of fermentation processes a novel computer programme was developed which is now commercialised and sold through a Dutch company. At present five to ten researchers work at the institute. The institute has collaboration to many European research institutions. These collaborations were initiated on a personal basis and on scientific conferences. Industry co-operations were established upon action of the industry. Though support for business-research co-operation exists at TTU it was not used by the institute, and its help is assessed as doubtful.

The Estonian food industry could be a relevant partner for institutes in the field of food technology. However, in the opinion of some interviewees there is a lack of experts for the industry as the TTU is relatively small and cannot teach the knowledge for all applications in the heterogeneous food industry.

Estonian Institute of Experimental and Clinical Medicine

The Estonian Institute of Experimental and Clinical Medicine was founded in 1947. Currently about 110 people are employed among them 50 scientists. Formerly the Estonian Institute of Experimental and Clinical Medicine was part of the Estonian Academy of Sciences; nowadays it is under the direct control of the Ministry of Social Affairs. The institute has focused its research in five departments

- Epidemiology and Biostatistics
- Oncology
- Environment and Toxicology

- Pulmonology
- Medical Virology

There was also a clinical department some years ago, that focused on clinical trials mainly to control imported drugs. However, this department was shut down. Clinical trials are now carried out on a contract basis with hospitals. In the case of epidemiological studies the institute has regular co-operations with the Medical Faculty of Tartu University. In the field of biotechnology the Institute of Experimental and Clinical Medicine has unique knowledge and study opportunities through its tissue database of cancers from Chernobyl victims. This project was financed by the US Cancer Institute by more than 15 million EEK. The institute could substantiate its important role in cancer research in Estonia if it was linked to other research facilities with the same thematic focus, e. g. by the combination of epidemiological studies and the molecular level in cancer research.

EVIKA Plant Biotechnology Research Centre

EVIKA was founded 30 years ago. Today it has seven employees. In the department of potato and the department of horticultural crops research is focused on plant biotechnological methods in diseases eradication, in improving disease resistance and yielding capacity of plants as well as in vitro methods in preservation of plant genetic resources. The gene bank contains now 417 varieties and 815 meristematic clones of the potato. Other species are e. g. plum, cherry, apple, pear, blue berry, and strawberry. Just recently a programme was started for the preservation of endangered Estonian orchids. Research facilities seem to be quite old and research is based on a more conserving level. Innovative methods are hampered by a lack of personnel and scientific equipment.

Key actors in biotechnological and medical research in the **Tartu region** are the Estonian Biocentre (EBC), various institutes of the Tartu University and the University Clinics as well as the Estonian Agricultural University.

Estonian Biocentre (EBC)

The Estonian Biocentre (EBC) was founded in 1986 as one of six genome centres in the former Soviet Union. For that purpose 91 million EEK were invested in new equipment, still the EBC remained in the old buildings. A new building for the EBC and the Institute of Molecular and Cell Biology (IMCB) was financed through the British Citrina foundation in 1996 with 30 million EEK. Additional money came through the PHARE programme of the EU. Nowadays the EBC is a joint venture between the Academy of Sciences and the University. Thus both personnel and projects of the Institute of Cell and Molecular Biology (IMCB) and the EBC are closely linked. Official publications mention 35 employees (14 researchers, 6 technicians, other infrastructural staff (librarian, computer and network specialists, etc) and 52 PhD students at the EBC. However, due to the close link to the IMCB the exact number of staff is difficult to determine. The annual report 2001 counts approximately 85 permanent employees with 9 professors, 56 scientists, 15 technicians and infrastructure personnel and 5 teachers for the EBC and the IMCB together. The EBC was selected in 2000 as "Centre of Excellence in Research in candidate countries under FP5" by the EU. This was connected to a financial aid of 4.6 million EEK for three years.

The main direction of research is molecular medicine, in particular activities in tumour biology, DNA-chip technology, genomic bioinformatics, and population biology. The EBC is involved in technological preparation of the Estonian Gene Heritage programme and facilitate development in other biotechnological directions such as gene therapy and DNA vaccination.

The EBC has good facilities and new equipment. However, on the basis of this good infrastructure efforts should be undertaken to intensify networking activities both within Estonia and abroad. Especially with the biomedical focus of its research collaborations to the Tartu Medical Faculty and the Tallinn situated KBFI should be intensified.

The EBC is intended to be part of a technology transfer strategy at the Tartu University. It is planned that ideas that are developed at the university are transferred into the bioincubation stage. The bioincubator as part of the EBC will consist of a preincubation centre. In this stage the idea is concretised for the spin-off activity mainly by literature research. This stage will also require the advice of external experts. Additionally, a high-level board of the bioincubator is intended to give advice to the start-up companies. After the preincubation stage the main incubator will host the spin-off companies for two to three years. The bioincubator will have laboratories with core technology (steam, pressure etc.), high-speed Internet links and a pool of major equipment such as spectroscopy and sequencing. Plans intend to end the planning phase by 2003 and finish the building in 2004. The investment costs are financed by the EU, the Estonian Ministry of Economic Affairs and Communications and the EBC. Running cost shall be covered by the rents to be paid by the start-up companies.

The idea of an bioincubator will close the existing gap between research and commercialisation. However, as plans for the bioincubator are still on the business plan stage an evaluation of the project is not possible at present. As critical points the number of expected companies, their financial capacities and the possible exit strategies of the start-up companies into the Biotech Park have to be monitored.

Tartu University

Key actors in the field of biotechnological research at Tartu University are the Institute of Molecular and Cell Biology, the Institute of Technology, and the Faculty of Medicine with its Biomedicum. The Ethics Centre at the Tartu University a virtual centre with the task to join the faculties of philosophy, medicine, law and biology.

Institute of Molecular and Cell Biology (IMCB)

The Institute of Molecular and Cell Biology (IMCB) at Tartu University was founded in 1990. According to the official number it consists of 24 researchers and 25 employees in the sector of technical infrastructure and for teaching. However, due to the close link to the EBC the exact number of staff is difficult to determine. The annual report 2001 counts 90 permanent employees with 9 professors, 62 scientists, 15 technicians and infrastructure personnel and 4 teachers for the EBC and the IMCB together. At present approximately 50 PhD students, 50 Master students and 250 undergraduates study in the field of bio- and gene technology. The research activities of the IMBC are focused on of molecular biology, gene technologies and molecular medicine. Most projects are in collaborations with laboratories in the USA, Europe and elsewhere and within Estonia (Estonian Biocentre, Tartu University Medical Faculty Tallinn Technical University, the National Institute of Chemical Physics and Biophysics). The IMCB was nominated Estonian Centre of Excellence of Research. This Centre was financed with 600,000 EEK in 2001 and 2002 by the Ministry of Education.

The Centre of Excellence for Gene and Environmental Technology (CGET) was organised on the basis of the IMCB together with the Institute of Zoology and Hydrobiology at Tartu University and the Institute of Technology. The CGET consists of the nine thematic groups biotechnology, cell biology, microbiology and virology, functional genomics, molecular biology, evolutionary biology, biochemistry, genetics, and plant physiology. These nine groups of the Centre of Excellence both represent the link between the University and the Estonian Biocentre.

Institute of Technology

The Institute of Technology (former Competence Centre for Technological Development) was founded in 2001. However, at present it is still fiction. Originally intended as a virtual institution to facilitate technology transfer at the university, the concept hat to be altered due to the lack of projects that focused on the technological development. Thus the institute will now provide both: the real research facilities with four centre (biomedicine, materials, IT, and environment) to develop basic research projects into ideas which can be commercialised and the support for technology transfer (writing of business plans, IPR, contact to investors, industry relations). The institute intends to create companies that are strong enough to be on the demand side for other spin-off companies to compensate the lack of big industry in Estonia. However, so far no success story can prove the practicability of this concept. On the other hand some interviewees from the group of SMEs criticised that the Institute of Technology at Tartu University does not focus on spin-off activities and/or technology transfer activities relevant for SMEs. The interaction of the Institute of Technology with the commercial side of biotechnology research should be one critical point for future monitoring activities to ensure success of the institute and enable the start-up activities.

Biomedicum

The Biomedicum is a centre for the pre-clinical programme and research work of the Faculty of Medicine. It was inaugurated in 1999, replacing scattered facilities of the Faculty of Medicine. It houses the Faculty's Institutes of Anatomy, Biochemistry, Pharmaceuticals, Physiology, Microbiology, Pathological Anatomy, Forensics, Healthcare, General and Molecular Pathology including more than 30 chairs or research groups. Additionally, it accommodates the State Agency of Medicines, a local forensics laboratory, and various service facilities of the Maarjamõisa Hospital (clinical autopsy, electronic microscopy and isotopes). The 190 million EEK investment costs were financed by a loan granted to the Republic of Estonia by the International Bank for Reconstruction and Development (IBRD) and from the national budget. The Biomedicum has excellent research facilities and high-level scientific equipment.

The focus of research varies among different groups. Some of them like the Institute of Microbiology have a strong focus on technology transfer. The department of microbiology has focused its research activities in the food sector on the improvement of human health through functional food. With research co-operations with companies and a patent in the field of strain development the institute has achieved a certain level within the Estonian biotechnology innovation system. Though the lack of strong industry is a hindrance for further commercialisation of the institutes products, to a certain extent the institute establishes its own demand by yearly seminaries for physicians in order to train on novel diagnostics.

Other institutes could have the potential to contribute their knowledge more actively into the biotechnology innovation system, especially in the field of clinical trial. Unfortunately, they tend to fail for various reasons such as lack of qualified staff and lack of qualified support by university technology transfer activities. In some cases the lack of transparency of the usage of overhead taken in by the university of all acquired grants was also mentioned as hindering factor for the provision of external money. The overhead costs at university sum up to 25 % at Tartu University which is rather high, especially if this is compared to only 3 % taken in by the university clinics. Another problem for some of the basic research institutes is the competition for qualified staff. Qualified researchers in this field are scarce and tend to choose a job in the pharmaceutical industry (often abroad) as wages in medical basic research at the university are low.

The overall impression is that the medical faculty has excellent research conditions. However, the different departments are of heterogeneous quality. To gain profit out of existing structures it should be ensured that innovative ideas are supported and university structures and university overheads do not hinder the development of personal activities in the acquisition of external money. Future co-operation between the medical and the biological faculty is crucial for the exploitation of the potentials of biomedical research.

Ethics Centre of the Tartu University

The Ethics Centre at the Tartu University was founded in 2001 as a virtual centre with the task to join the various faculties. Involved are the faculty of philosophy, medicine, law and biology. The centre has a board and an international committee. The Ethic Centre's staff is mainly financed from the co-operating faculties. Only two infrastructural employees care for the library, the dissemination of publications etc. The Ethics Centre is supported by the VW foundation with support of the University of Constance with 1.6 million EEK for three years. So far no joint research projects were initiated with the Biological and Medical Faculty at Tartu University as the ethical reflection of present research projects was not asked for. Similarly biotechnology companies are sceptical to involve the Ethics Centre. There is one international research co-operation with the University of Constance and several international research projects within the fifth framework programme of the EU. Researchers from Iceland, Sweden (Lund), UK (Lancaster, Lancashire) and the Ethic Center co-operate in the project ELSAGEN (Ethical, legal Issues of Genetic Databases). Networking activities are financed through the Nordic Academy of Advanced Studies within the NorFa project in co-operation with Iceland, Sweden and Finland.

At present the work of the Ethics Centre is mainly concentrated on the organisation of workshops and seminaries with high-level international experts. However, the public interest in these activities on this offer is relatively small. The best way of critical discussion seem to be anonymous Internet platforms.

In the view of the Ethic Centre's the regulations of the Estonian Genome Project are very progressive and allow the protection against genetic discrimination. However, there are aspects especially in terms of data protections that are unsolved. Among them is the question how the volunteers can profit out of their gene donation if family doctors have to give away all personal data related to the gene donor.

Estonian Agricultural University

The mission of the Agricultural University is to guarantee sustainable use of natural resources and enhance rural development. In 1987 the Estonian Agrobiotech Centre was founded within the Agricultural University. The Agrobiotech Center is the relevant institute for biotechnological research with a focus on animal health. It employs nine scientists and eleven technicians. Research activities focus on the development of autogeneous animal vaccines, diagnostic kits for agriculture and other bioproducts (sera). The Agrobitoech Centre finances its research by money from the Ministry of Education and the Ministry of Agriculture (both approximately 400,000 EEK) and by the sale of the institute's products (1.5 million EEK) to the Estonian market. Due to the production conditions that do not fit international GMP standards the Agrobiotech Centre cannot expand its commercial activities to other countries. The renovation of the institute's facilities is intended for the next three to five years but financing is not ensured for this activity.

To support the development of this sector of biotechnology in Estonia the Agrobiotech Centre should put more effort on international visibility through publication and networking activities and invest in education.

University Clinic

The Tartu University Clinic consists of 17 departments (clinics) that vary in size between 10 and 80 physicians and a capacity of 30 to 100 beds. The University Clinic is linked to the Tartu University through the physicians: approximately one third of the physicians has both a job at the university clinic and at the Faculty of Medicine of the Tartu University. 15 out of 17 senior physicians are both head of a clinic and professor at an institute at the related university department. Research activities are carried out at the University, the clinic guarantees the access to the patient (preclinical research is carried out at the university, clinical research at the university clinic). 30 to 35 clinical studies are carried out at the University Clinic per year.

Research co-operations exist mainly with the Medical Faculty of the Tartu University, and to some extend with the Biological Faculty of Tartu University. International research co-operations exist on a personal level between single department (e. g. the children's cardiology co-operates with the Charité in Berlin). Co-operations with Estonian companies are rare and are more characterised by a customer relationship. One example is Quattromed which supplies the university with clinical diagnostics. Big international pharmaceutical companies are sponsors for clinical trials. The University Clinic favours clinical trials for several reasons. The earnings of clinical trials is added by 90 % to the income of physicians and nurses, involved in the clinical trial. As the income of the clinic personnel is rather low this practice helps the University Clinic to increase the salaries. Pharmaceutical companies that have clinical trials conducted at the university clinic pay for travel expenses to attend international conferences and guarantee the further education of the personnel. Thus, the personnel both learns systematic work and gets international experience. The board of the clinic does not fear a conflict of interest due to this close monetary linkage as in their argumentation the patients are examined and treated in any case.

Interviewees stated that the regulatory framework for the clinical research at the University Clinic is mainly acceptable. Approval for clinical studies occur normally within two to three months, the target is to limit this time to a six week period. Problems for the clinical research activities result from the data protection regulations.

There are two research initiatives in Estonia with a nation-wide focus. These are the Estonian Genome Project Foundation and the Estonian Academy of Sciences.

Estonian Genome Project Foundation (EGPF)

The Estonian Genome Project Foundation is a non-profit organisation founded by the Government of the Republic of Estonia for the preparation and implementation of the Estonian Genome Project. The Estonian Genome Project was initiated in 1999. The objective of the Estonian Genome Project is to establish a database of health and genetic data of the people of Estonia that enables more exact and efficient diagnoses of a disease, improvement of treatment and determination of risks of the development of an illness in the future. In order to ensure the correct handling of data in terms of personal, ethical and juridical aspects the Human Genes Research Act was enacted by the Estonian Parliament in December 2000. The Human Genes Research Act regulates the establishment and maintenance of a gene bank and collection, processing and insurance of data. In March 2001, proceeding from the Human Genes Research Act, the Government of the Republic founded the Estonian Genome Project Foundation (EGPF) that belongs in the area of administration of the Ministry of Social Affairs. Today there are 24 people employed at the EGPF. As teaching of the participating family doctors will increase in 2003 as soon as the main phase of the project is started, the foundation intends to employ more personnel in 2003.

The commercial part of the Estonian Genome Project is EGeen Ltd. (EG), which is a public limited company founded by the EGPF in April 2001. EGeen carries out the financial-economic objective of the Genome Project. In order to organise the contact to international investors, EGeen International was founded in the United States. Although at the time of the personal interviews in October/November 2002 only a few hundred blood samples have been collected in the Estonian Genome Project, EGeen already tries to commercialise the project, not least to fulfil the expectations of its venture capital investors (see chapter 2.2.3). The main business strategy of the company is the development of pharmaceutical and health care products based on the collected genomics, proteomics and health data, in particular individualised medical solutions. In addition, EGeen tries to find co-operation partners in the pharmaceutical industry which are interested and able to validate drug target candidates and genetic drug profiles. In order to provide the necessary basis for starting commercialisation activities of the Estonian Genome Project, it seems necessary to increase the number of collected blood samples and the speed of sample collection enormously in 2003 and the coming years. Otherwise it cannot be excluded that the expectations of interested pharmaceutical companies cannot be fulfilled due to lack of data or collected blood samples. Furthermore, the target of EGeen to develop to a (integrated) biopharmaceutical company seems to be rather ambitious and its chances of success cannot be assessed at the moment. However, it should be taken into account that substantial amounts of investment capital and a time frame of at least five years are required to develop validated drug candidates. In addition, most of the new entities fail during the drug development process, so that a high risk is included in this strategy as well. In this sense it seems advisable to carefully check the possibilities of more service-oriented business activities related to the Estonian Genome Project, not least because a lot of such activities can be carried out in Estonia.

Compared to other human genome project initiatives the Estonian Genome Project is unique as it is focused on the collection of a huge amount of data of healthy people. In contrast, the Iceland genome project carried out by DeCode, applies the traditional linkage analysis in selected disease. The Estonian Genome Project thus expects to create an enormous data pool with multiple analytical options. The Human Genes Research Act is internationally accounted as a progressive law that allows efficient protection of personal rights. However, up to now certain aspects seem to be not sufficiently worked out e. g. the accessibility of personal data by the gene donors. On the other hand the commercial exploitation of the data has not yet started and problems that may arise from this cannot be foreseen at the moment. For example, if appropriate candidates for clinical testing or personalised therapies shall be chosen based on information collected in the database, this selection would on the other hand violate the individual rights of the selected candidates.

Estonian Academy of Sciences

The Estonian Academy of Sciences acts to shape science and research policy, it comments on related laws, represents the Estonian science in international committees, and publishes peer reviewed journals (however, no journal with biotechnological background).

According to the New Act on the Estonian Academy of Sciences (1997) the Academy has personal members and has few own research institutions. Among them are with a life science background the National Institute of Chemical Physics and Biophysics, the Estonian Biocentre, and as associated member the Institute of Zoology and Botany of Estonian Agricultural University.

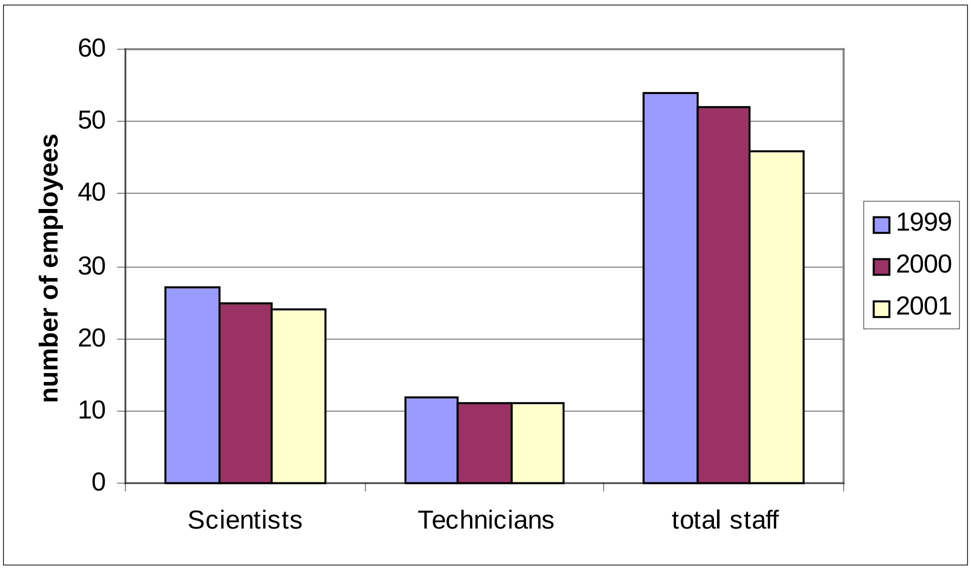
To increase public perception of science two series of seminaries are carried out with the focus on "Sciences for Society" and "New Trends and Science" by the Academy of Sciences. However, the public interest is often rather low even though well-known institutes and speakers are invited. Information material is published on the basis of the public lectures by the Academy as well.

2.1.2 Staff structure

18 key actors of research institutions in Estonia have been interviewed and were asked to fill in a data sheet in order to analyse structural characteristics of the Estonian biotechnology innovation system. Until 4th of December 2002 we received seven data sheets, which equals to a response rate of 39 %. This enables us to give first conclusions, still results are not statistically significant. In conjunction with the picture gained on a qualitative basis from the personal interviews an overall insight of the structural and thematic characteristics of the research institutions is possible.

The size of research institutes that answered the questionnaire varied between a minimum staff of 10 in 1999 and a maximum staff of 174 in 1999. However, the majority of institutes (5 out of 7) were in the range of 11 to 25 persons in 2001 and only two institutes had a personnel capacity higher than 100 persons. Smaller institutes (up to 25 people) had a constant number of employees, whereas the bigger institutes (more than 100 employees) experienced a decrease in staff during the last three years. Thus, the average staff number in all answering institutes decreased by 15 % (figure 2.1). Regarding the proportion of scientists and technicians there are two to three times more scientists than technicians in the answering research institutions. All institutes had scientific personnel with a biological and chemical background and technical staff. Two thirds had staff with a background in medicine, one third had administrative personnel. Other scientific background mentioned was economy, social science, administration, clinical trials, engineering and agronomy.

Figure 2.1: Average number of staff at Estonian research institutes



Source: Fraunhofer ISI 2002

2.1.3 Co-operation activities

In general, the relevance of co-operation is assessed as very high by the Estonian research institutes. Despite this opinion, three of six research institutes gave an 'unfavourable' evaluation of the business-to-business co-operation, one assessed it as 'average' and two as 'favourable'. The research-to-business co-operation was assessed by the majority (n=4) as unfavourable, one assessed it as 'average' and two as 'favourable'. The evaluation of the availability of research facilities in Estonia was more diverse, it reached from two votes for 'unfavourable' and three for 'average' to two persons who assessed this framework condition as 'favourable' and 'very favourable'.

Public programmes to assist the establishment of co-operation relationships are described as not very helpful, an assessment that one interviewee extended to the respective offerings made by the EU. More effective are personal contacts, e. g. resulting from former studies or research stays abroad, possibly sponsored by scholarships. Personal contacts to international partners are especially relevant for the application for funding by the EU. Several interview partners added, that international publications and visits at international conferences are also very helpful to establish co-operations. In some cases, the work for foreign firms as a subcontractor initiated independent contacts to new co-operation partners.

Co-operation partners

Most of the co-operation relationships of the research institutes are arranged with other research institutes (60 % or co-operations), followed by SMEs and other institutions (such as service providers and financing facilities) with around 20 % of the relationships each. The spectrum is quite similar to the co-operation partners of the research institutes in the Hanover region (Menrad et al. 2001) except the fact that no partnerships to large firms are reported for the Estonian research institutes, whereas 16 % of the German research institutes co-operated with large firms. Estonian research institution are experiencing problems especially in finding industrial co-operation partners both within Estonia and abroad. The reason for this fact is the lack of strong big Estonian industry mainly in the chemistry, pharmacy and advanced food sector. Abroad the difficulties in finding industrial co-operation partners are accounted to a lack of information within the targeted industry due to the geographical distance from Estonia to the EU.

From the viewpoint of some researchers co-operation relationships with industry partners are sometimes not easy to realise. The universities were said not to have a good strategy for the co-operation with industry partners and a lack of experience was stated in the university technology transfer programme. Persons with special knowledge left the university to work in enterprises what results in a deterioration of the quality of education.

Most of the co-operations were built up in 1997, single ones reaching into the past until 1950. The peak in co-operation activities in 1997 may be due to the fact that Estonian research institutions became actively involved in projects of the EU FP5, which started in 1998. In preparation of the EU proposals the collaborations may be established the year prior to the start of the research activities. This illustrates the importance of the EU research activities for Estonian research institutions not only from a financial point of view but only from a scientific knowledge aspect.

Since 1998, between one and seven new relationships could be newly established. Most of the co-operation partners are settled in foreign countries (n=20 or 44 % of the co-operations), followed by the Tallinn region (29 %), Tartu region (20 %) and the rest of Estonia. The origin of the foreign partners is shown in table 2.1.

Table 2.1: Origin of foreign co-operation partners of research institutes

Country	Frequency
Sweden	6
Sweden	6
Finland	4
Finland	4
European Union	2
European Union	2
USA	1
USA	1
United Kingdom	1
United Kingdom	1
Switzerland	1
Switzerland	1
Netherlands	1
Netherlands	1
Latvia	1
Latvia	1
Germany	1
Germany	1
France	1
France	1
Canada	1
Canada	1

Source: Fraunhofer ISI 2002

As table 2.2 reveals, most of the co-operation relationships exist to partners outside Estonia. Inside Estonia, the research institutes from Tallinn find their partners mostly in their own region. Research institutes from Tartu have fewer co-operations (13 all in all), four of the national contacts exist inside the Tartu region, two to partners from Tallinn and one to a partner in the rest of Estonia. This concentration on research co-operations within the region was highlighted in the interviews as well and explained by a certain "competition" between Tallinn and Tartu in the biotechnology field.

Table 2.2: Regional distribution of co-operation relationships of research institutes

		Origin of co-operation partner				
		Tallinn	**Tartu**	**Rest of Estonia**	**Outside Estonia**	**Sum**
Region of research institute	Tallinn	11	5	1	13	30
	Tartu	2	4	1	6	13
	Rest of Estonia			1	1	2
Sum		13	9	3	20	45
Multiple responses, k=45 co-operation relationships of n=8 research institutes						

Source: Fraunhofer ISI 2002

National collaborations, for example between research institutes in Tallinn and Tartu, sometimes suffer from a lack of financial support, whereas international contacts are in part sponsored by foreign funding institutions. In some cases, foreign partners e. g. from Finland or Sweden offer services for prices that are comparable to those of Estonian firms, and often their services are more reliable and in-time than those of national suppliers.

Areas for co-operations

The most widespread tasks for which co-operation relationships are established by the research institutes are the solution of scientific questions (60 % of the institutes claim this type of co-operation), followed by product development and financial questions (table 2.3). Marketing or distribution, the arrangement of other co-operations, contract manufacturing or clinical trials, business consulting and other purposes are less relevant.

To compare these results with the research institutes in the region of Hanover (Menrad et al. 2001), the co-operation relationships of both the Hanover and Estonian research institutes have their main focus on scientific research, but product development and financial questions play a more important role in Estonia.

Table 2.3: Purpose of co-operation relationships of biotech research institutes

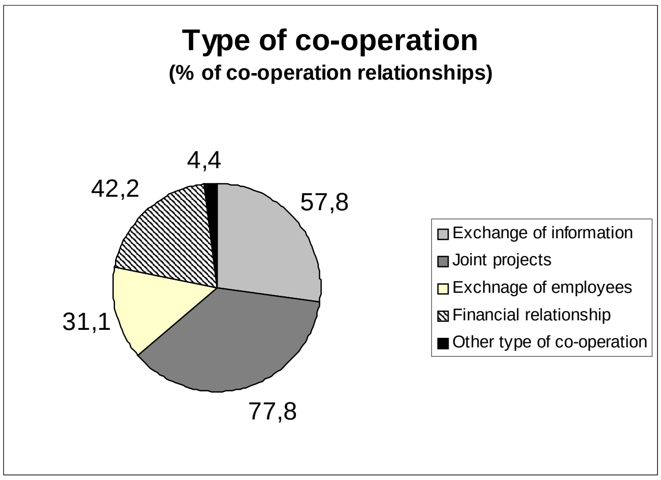
Scope of co-operation	**% of institutes**
Scientific questions	60.0
Product development	33.3
Financing of company	20.0
Marketing/distribution	6.7
Arrangement of co-operation	6.7
Contract manufacturing/ clinical trials	2.2
Business consulting	2.2
Other Purpose	4.4
k=45 co-operations of n=8 companies, m=61 responses	

Source: Fraunhofer ISI 2002

Co-operation activities

Nearly 80 % of the co-operations of Estonian biotech research institutes to their partners are joint projects, nearly 60 % of the relationships (also) have the character of information interchange. A bit less prevalent are co-operations in the form of financial relationships or the exchange of employees (figure 2.2). Because a single co-operation partnership can have several aspects, the percentages in the figure 2.2 sum up to more than 100 %. In comparison to the Hanover region (Menrad et al. 2001) it can be seen that for the Estonian research institutes financial relationships are of a relatively high relevance.

Figure 2.2: Type of co-operation: Research institutes



Multiple responses, k=45 co-operation relationships of n=8 research institutes

Source: Fraunhofer ISI 2002

International contacts of the research institutes are important to give their students the opportunity of a stay at a foreign laboratory, which is often sponsored by scholarships.

Activities to improve co-operation

The research institutes proposed the following actions to improve the framework conditions for co-operation partnerships:

- Support is necessary for the participation at conferences to establish contacts to other institutions.
- The search for co-operation partners should be supported more effectively.
- Generally, Estonia should be marketed more actively as a technology site.
- Because of the highly interdisciplinary character of biotechnology and genetic engineering, the co-operation of very different institutions and disciplines should be promoted, for example between biotech companies and IT-specialists.
- To enforce co-operations it should be assured that IPRs and other special knowledge are safeguarded in contacts between different and especially between competing institutions.

2.1.4 Structure and development of research funding related to biotechnology

Financing of research in Estonia is limited through the fact that only 0.75 % of GDP are spent on research, with 80 % out of this from public sources. Generally there are five different sources to finance research activities at research institutions

- Estonian Science Foundation,
- Ministry of Education,
- Estonian Technology Agency,
- European Union,
- private trusts (e. g. VW Foundation, Wellcome Trust, Citrina Foundation).

Apart from these national and European funding opportunities there are some regional activities, especially in respect to technology transfer (SPINNO project at Tallinn Technical University) and the hiring of qualified staff (repatriation fund in Tartu).

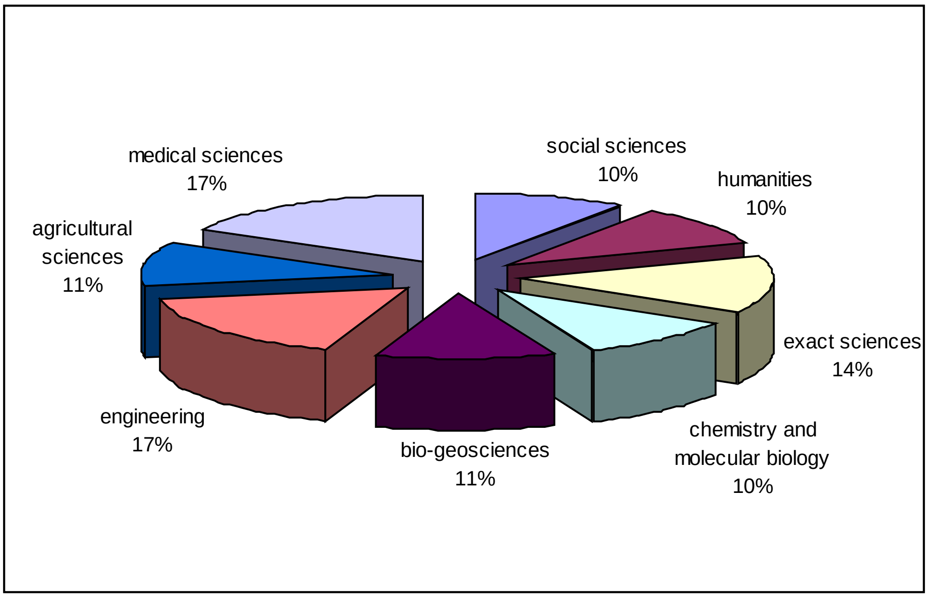
Up to now there was no specific biotechnology funding programme in Estonia. In contrast, the Ministry of Health had specific programmes for medical research, the Ministry of Agriculture focused on agricultural research, the Ministry of Economic

Affairs and Communications finances research projects in companies and public institutions.

Estonian Science Foundation

The Estonian Science Foundation (EstSF) was founded in 1990 in order to organise the distribution of research funds. After the establishment of the Science Competence Council at the Ministry of Education in 1998 with responsibility for the target-oriented projects, the EstSF administers around 20 % of the research budget of the Ministry of Education (= 72 million EEK). The major tools of the Estonian Science Foundation are grants to support promising initiatives in all fields of basic research and scholarships for young scientists. The distribution of grants in 2001 can be seen in figure 2.3.

Figure 2.3: Distribution of EstSF grants by fields of science in 2001



Source: Estonian Science Foundation 2002

The grants of the EstSF are rather small and have a short-term perspective (one year). This short-term projects are oriented upon scientific quality based on peer evaluation. However, in the view of many of the interviewed researchers these grants are often only relevant to send people regularly to international conferences or to pay a technician of it. Long-term research cannot be conducted with this financing instrument.

Some grants for interdisciplinary research projects are available at the Estonian Science Foundation as well (approximately 20 % of all projects). Often these projects do not pass the subject-specific evaluation committees of EstSF as some interviewees criticised. Specific difficulties of interdisciplinary research projects arise through differing cultures and languages of the various scientific disciplines, lack of know-how of discipline-oriented evaluation committees in parts of the research project as well as the fact that interdisciplinary projects often gain their added value through the interaction of scientists of different disciplines but do not represent high-end science in the involved disciplines. Thus, financing problems may arise for interdisciplinary research projects. As these projects seem to be extremely important to further develop the science base in Estonia not only in the life science field, a special committee at the EstST is intended to combat the financing problems of interdisciplinary projects.

Ministry of Education

Funding through the Ministry of Education is carried out by the Science Competence Council, the advisory committee of the Ministry of Education for basic and applied research. The Science Competence Council consists of nine members of the scientific community with long experience in project acquisition and management. Main task is the evaluation of research projects, that are submitted to the Ministry of Education. Target-oriented projects (target grants) are open to researchers of all disciplines and can be funded with a perspective of up to five years with a total volume of two to three million EEK. The evaluation process tries to engage anonymous reviewers. In general, the Science Competence Council follows the views of the reviewers. According to interviewees' statements 90 % of the evaluation reports of reviewers for the project proposals are clear. In case of conflicting views of the reviewers the Science Competence Council either asks for additional external reviewers or takes a decision immediately. Within the last years two additional programmes were initiated by the Ministry of Education and the Science Competence Council:

- Post-doc programme that allows doctoral students to apply for a two-year scholarship with a volume of 200,000 EEK/year. This programme allowed the financing of approximately 20 post-docs. Interviewees assessed the quality of the programme as high since some of the students spent part of their post-doc time abroad. The programme is intended to be changed as to allow also institutions to apply for a post-doc position.
- Centre of Excellence in Research Programme: This programme was initiated by the Ministry of Education. The practical handling of the programme and the evaluation of the respective Centres of Excellence is assisted by the Science Competence Council. Seven Centres of Excellence have been chosen two years ago. The Estonian Biocentre, the Centre of Excellence for Gene and Environmental Technologies in Tartu and the Centre of Excellence of Analytical Spectrometry with its Functional Genomics and Proteomics Group in Tallinn are among them in the life science sector. At the beginning of the programme funding was intended for two years. However in the meantime, the prolonged funding for the next five years with increased amount of money seems to be

decided. Several interviewees criticised that no evaluation has been carried out so far concerning the selection procedures and criteria of the Centres of Excellence as well as the impact of the programme. Further criticism arose concerning the fact that the duration of the programme has been prolonged substantially as well as the budget spent for this programme without evaluating the interim results of the existing Centres of Excellence in detail. In this context most interviewees stated that with an overall amount of 7 million EEK for the seven Centres of Excellence for the years 2001/2002 the budget is too small to achieve relevant results. This estimation was agreed by some scientists participating in Centres of Excellence in the life sciences field, who mainly use these funds for travelling to international conferences (often also for PhD or post-doc students), educational purposes or maintaining the technical infrastructure.

Estonian Technology Agency (ESTAG)

One of the objective of the Estonian Technology Agency (ESTAG) is to assist Estonian research institutions in conducting technology-related and innovative feasibility studies and applied research. There are two instruments to finance projects with grants:

- Financing of feasibility studies: up to 75 % of total costs
- Financing of applied research: up to 100 % of total costs

Most of the projects are joint projects between companies and research institutions, in particular since the development of such co-operations themselves is seen as one of the objectives of the ESTAG. Since 2001 the ESTAG runs the SPINNO programme that is intended to increase the technology transfer from university to industry. A detailed description about this programme and ESTAG's activities is included in chapter 3.3.

From the point of view of the interviewed researchers the ESTAG application is rather demanding in terms of details that have to be worked out. However, some interviewees stated problems with confidentiality of data provided by the project proposals in particular if ESTAG sends the proposals to an Estonian expert for evaluation.

EU-Funding

EU funds are of high importance for the academic research in Estonia. Within the 5th Framework Programme a total amount of 256 proposals were submitted to the EU in the Quality of Life Programme of which, whereas proposals for financing were made to 54 projects. This represents a success rate of 21 %. Among the successful projects 66 % were submitted from Tartu, and 25 % were submitted from

Tallinn. Only 9 % were submitted from institutions situated in other regions. The biggest achievements in terms of structural importance might be the attainment of two Centres of Excellence projects at INCO II project competition. One of the two European Centres of Excellence is the Estonian Biocentre. This is a success that boosts directly the Estonian efforts outlined in the national strategy "Knowledge-based Estonia". In total, Estonian research was financed by a sum of nearly 156 million EEK from the Quality of Life-Programme in FP5 (Archimedes Foundation 2002).

To support the application activities the National Contact Point (NCP) host organisation Foundation called "Archimedes" carries out information dissemination, consultancy and partner search. Additionally, a continuous information flow is organised through the website of Foundation Archimedes.

Regional Funding

Due to the activities of regional institutions, mainly the Tartu University and Tallinn Technical University, there are special financing instruments restricted to a region. In the case of the Tallinn Technical University the University successfully applied for a project funding within the SPINNO programme. This project aims at assisting technology transfer activities of the University. In the case of the Tartu University a special repatriation fund was initiated that allows the university to pay salaries to researchers coming back from abroad for a two years period.

2.1.5 Financing situation of research institutions

The number of externally financed projects in the institutions filling in the data sheet varied between two and 38. There is a slight increasing of external project financing from an average of 11.4 projects/institute in 1999 and to 13.8 projects/institute in 2001. The answering institutions had the impression that the relevance of external project funding had increased or at least remained the same since 1999. The annual institute budget varied in 1999 between 1.45 million EEK and 20 million EEK, in 2001 between 1.7 million EEK and 30 million EEK. The average budget of the six answering institutions rose from 6.6 million EEK in 1999 to 8.6 million EEK in 2001. Taking the inflation into account the net average annual budget of the research institutes rose by 7.1 % in 2000 and by 10.2 % in 2001. These numbers are relatively high and illustrate the efforts which are undertaken to support biotechnological research in Estonia (table 2.4). The share of the institute's budget spent for biotechnology research varied between 20 % and 100 %.

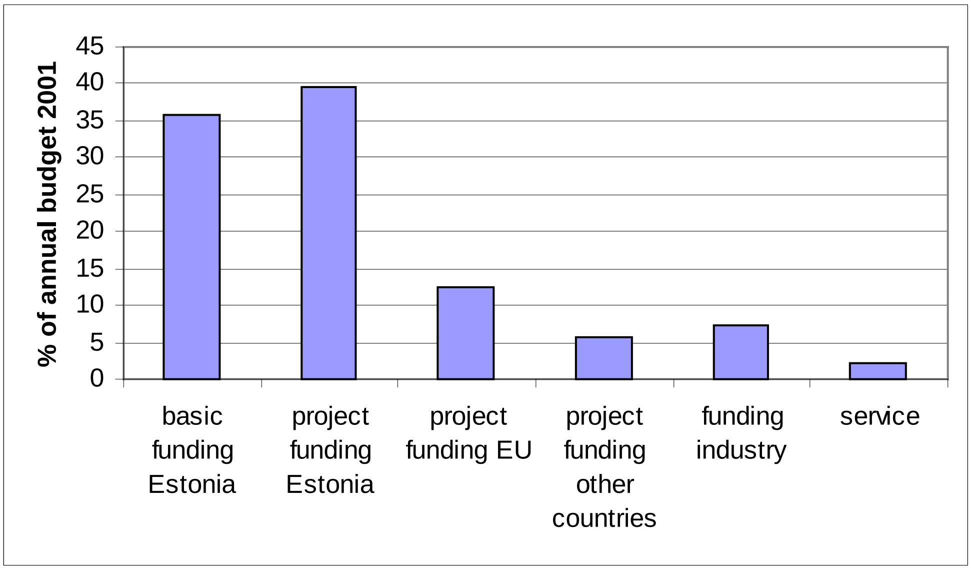
Table 2.4: Financial situation of research institutes

	1999	2000	2001
Annual average budget (mio EEK)	6.628	7.377	8.582
Inflation rate	3.1 %	3.9 %	5.5 %
Net increase	-	7.1 %	10.2 %

Source: Fraunhofer ISI 2002

In the interviews with 18 key actors from research institutes the impression was given that biotechnology-related research projects are equally financed by Estonian funding and EU funding. Taking this, 40 % to 50 % of research was carried out on EU funds. Taking the overall financial situation of the institutes that answered the questionnaire, which includes both expenses for teaching and research, 35 % of the average annual institute's budget originates from basic public funding. Nearly 40 % originates from Estonian project funding and 12 % are research funds of the EU, 6 % national funds others than Estonian ones (e. g. USA, Sweden, Finland), and 7 % originate from industry, contract research or clinical trials and service. Contract manufacturing or counselling contributes only with 2 % to the total institute's budget (figure 2.4).

Figure 2.4: Origin of total average annual institute's budget (%).



Source: Fraunhofer ISI 2002

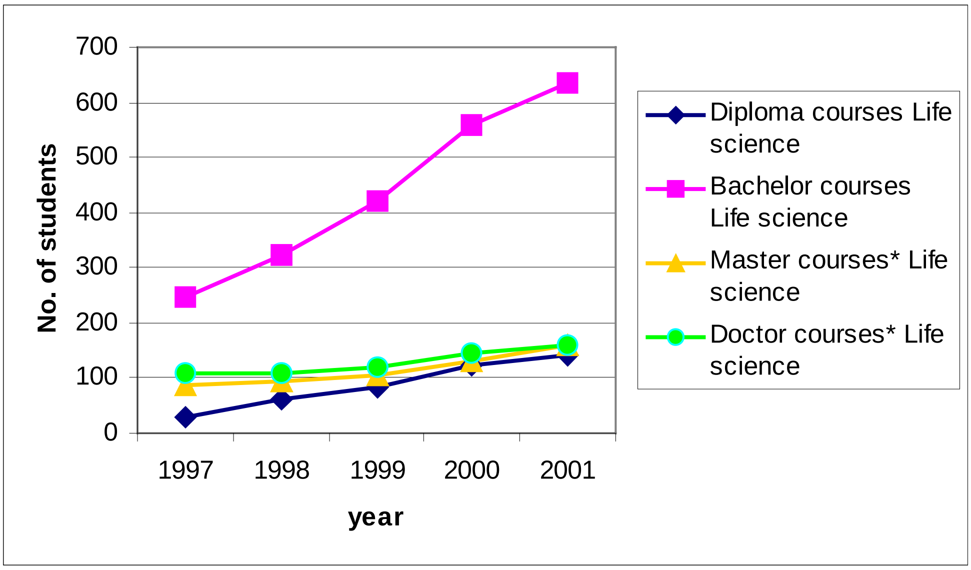
The discrepancy between the information about the importance and the contribution of EU money for the total institute's budget given during the interviews and the answers in the questionnaire may result the fact that only part of the research institutes answered the data sheet and/or the different perception of the relevance of research projects and their actual contribution to the budget.

2.1.6 Education and training possibilities

During the last years Estonia experienced a shift within education and training possibilities which influenced the availability of qualified staff. All interviewed research institutions were able to recruit graduates and postgraduates with relevant biotechnology knowledge and skills. However, in many cases there was no real choice in candidates, but one application for one position. The major problem to get qualified staff is the salary research institutions are able to pay. According to information given during the interviews salaries at research institutions are only 60 % of those paid in industry and public agencies. The availability of qualified technical staff seems not as good as the scientific personnel. Most of the interviewees tend to train their technical staff on the job. As told by one interviewee the vocational training for technicians is mainly theoretical and lacks sufficient practical education in the lab. Often bachelor students are mobilised for technical work in the laboratories as well.

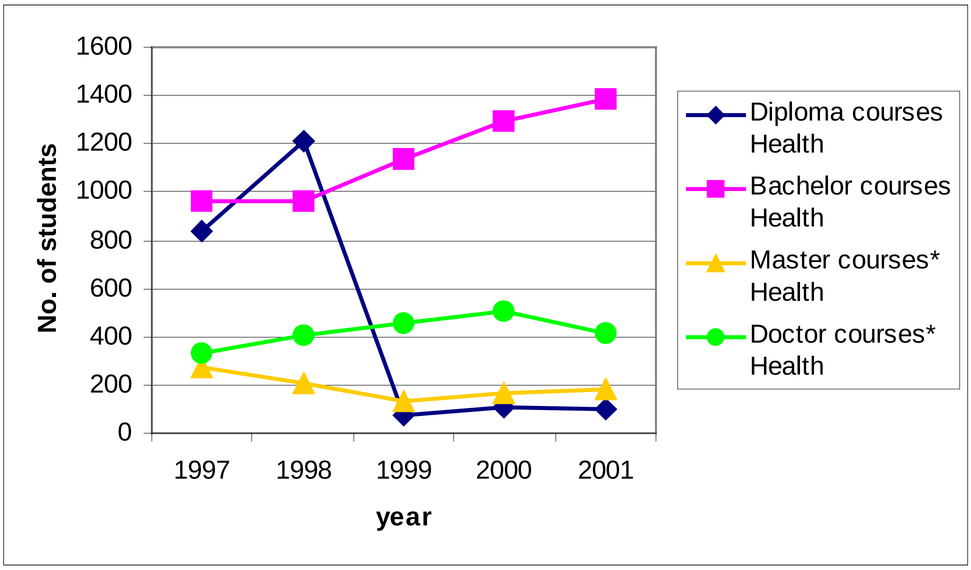
Analysing the number of students in disciplines related to the biotechnology innovation system elucidates a trend that may be problematic for the further scientific and commercial development of biotechnology in Estonia. On the one hand, the number of students in the life science sector rose constantly during the last years (figure 2.5). On the other hand the increased number of undergraduates did not lead to a proportional increase in graduate students. According to interviewees there are often financial reasons as well as a limited interest of students in scientific work which prevent that master students start a PhD thesis. In addition, the observed discrepancy may be explained by a certain enthusiasm for biotechnology that was transported through the media in relation with the Estonian Genome Project and motivates studies in biotechnology-related disciplines. However, this enthusiasm leads to a problem if students are faced with scientific reality and its non-exiting daily routine as one interviewee told. At present it cannot be foreseen if the increased number of bachelor students since 1998 will proportionally lead to the same development in PhD students in the coming years. In the case of medicine the number of undergraduates rose as well, however, the number of PhD students decreased between 1997 and 2001 (figure 2.6).

Figure 2.5: Student numbers in life science courses



Source: Statistical Office of Estonia 2002; (* Master courses include internship enrolment and doctor courses include residentship enrolment)

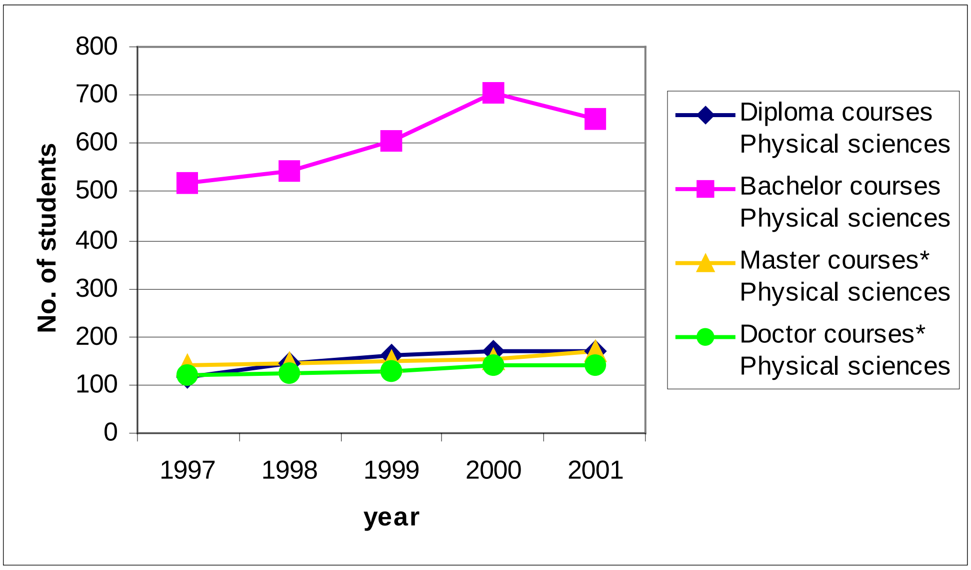
Figure 2.6: Student numbers in medicine



Source: Statistical Office of Estonia 2002 (* Master courses include internship enrolment and doctor courses include residentship enrolment)

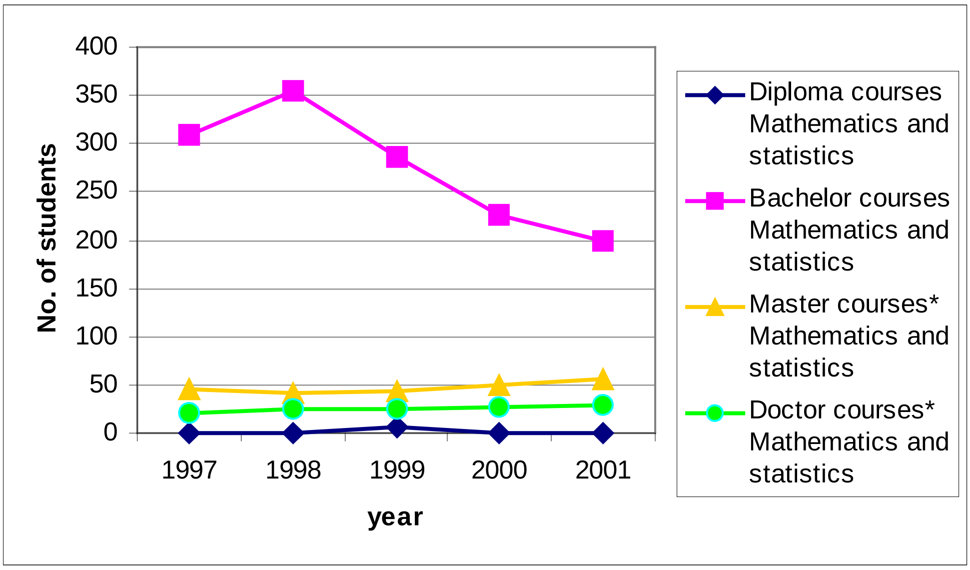
Both undergraduate and graduate student numbers in physics and mathematics decreased (figures 3.17, 3.18) in the last five years. This trend was agreed during the interviews and seen as problematic for the mid-term development of biotechnology as well as its potential application industries. The situation in chemistry courses was similar to the trend in physics and mathematics. As interviewees told there is low interest for natural science among students having passed their baccalaureate. As a consequence industry seeks already chemically trained specialists.

Figure 2.7: Number if students in physical sciences



Source: Statistical Office of Estonia 2002 (* Master courses include internship enrolment and doctor courses include residentship enrolment)

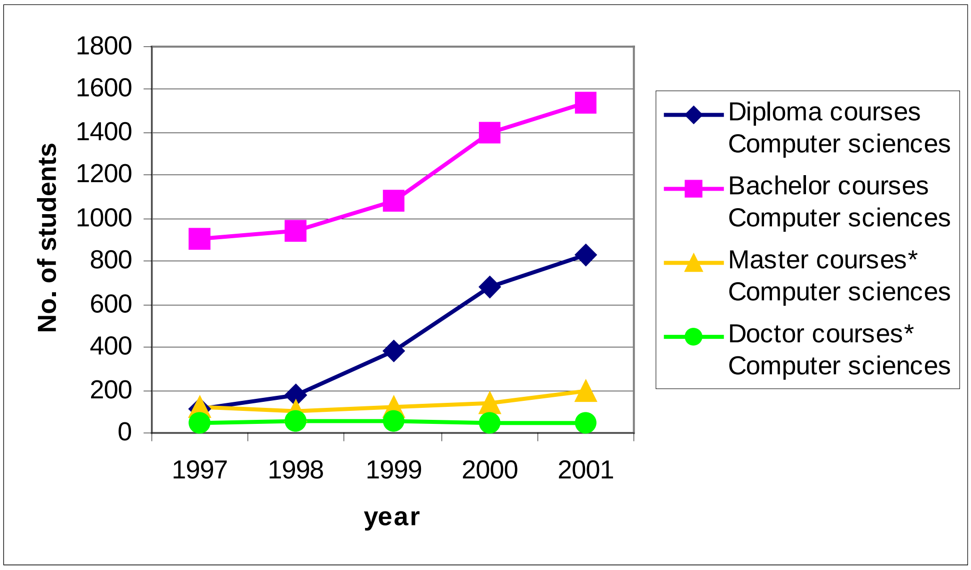
Figure 2.8: Number of students in mathematics and statistics



Source: Statistical Office of Estonia 2002 (* Master courses include internship enrolment and doctor courses include residentship enrolment)

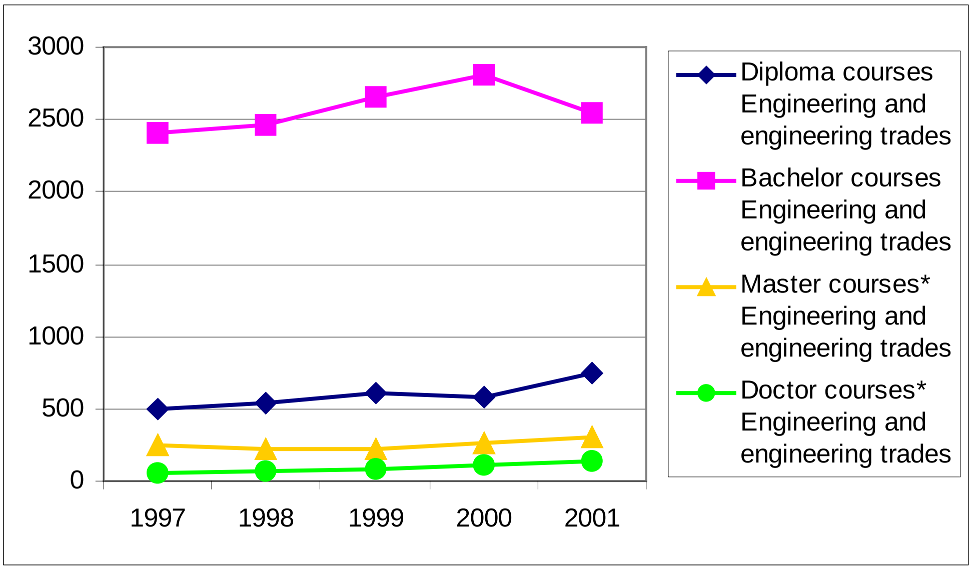
Almost similar to the life science area is the development in students in the field of informatics. With strongly increasing numbers of undergraduates a relatively moderate increase of master and PhD student in informatics can be registered in recent years (figure 2.9). This development most probably was influenced by the rather positive development of the IT industry in Estonia in the recent years. Similar trends can be registered in other European countries.

Figure 2.9: Number of students in informatics



Source: Statistical Office of Estonia 2002 (* Master courses include internship enrolment and doctor courses include residentship enrolment)

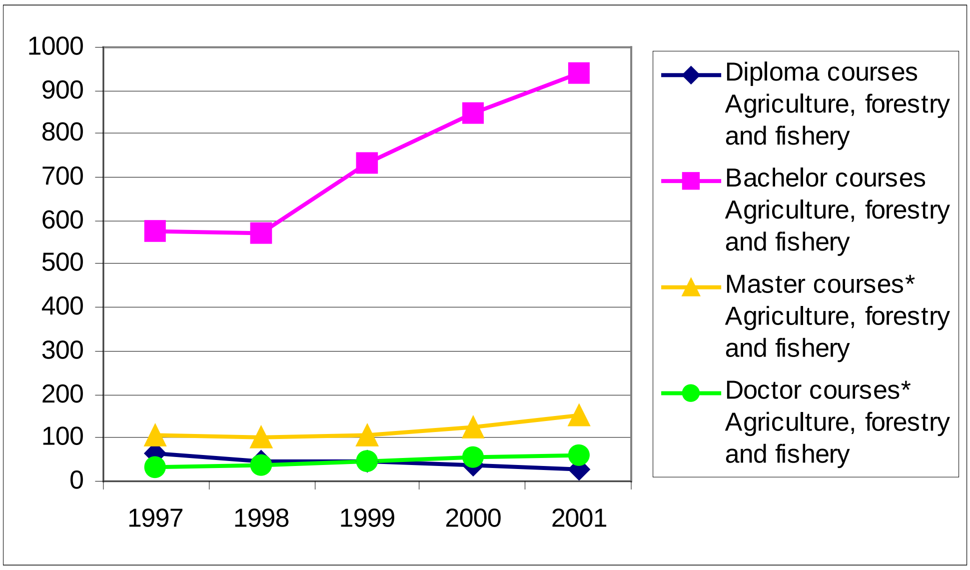
Figure 2.10: Number of students in engineering



Source: Statistical Office of Estonia 2002 (* Master courses include internship enrolment and doctor courses include residentship enrolment)

Finally, the number of students in engineering shows an increase in undergraduates until 2000 and at present a decrease, connected with an increase in PhD students (figure 2.10). Though the number of students in bachelor courses in agriculture, forestry and fishery has increased during the last years, in this case it must be stated that the curricula must be adapted to fulfil the requirements of modern innovative plant biotechnology research (figure 2.11).

Figure 2.11: Number of students in agriculture, forestry and fishery



Source: Statistical Office of Estonia 2002 (* Master courses include internship enrolment and doctor courses include residentship enrolment)

An overall trend is that many students do not continue their studies after the bachelor. As the bachelor courses teach mainly theoretical knowledge and the master courses are often seen as preparatory phase for a PhD course university graduates often lack industry-relevant knowledge and specialised engineers and scientists are scarce in Estonian industry. This was seen as a major problem e. g. for the food or chemical industry of Estonia. On the other hand industry has hardly any strategies for internal qualification schemes and strategies for personnel development. The low number of PhD students is ascribed to the low salaries at university and the small number of grants available in Estonia. Often the best students prefer either a doctoral position abroad or they leave for a position as sales representative and thus are lost for research as some interviewees pointed out.

In contrast to higher education which has adapted its curricula partly to the demands of market and the new focus of "Knowledge-Based Estonia", the vocational training in Estonia does only follow the demand of companies in exceptional cases. There is a huge number of vocational schools in Estonia, which are scattered all over the country. In the opinion of some interviewees the number of schools should be substantially reduced and the new schools should be strategically reorganised. In fact employers at research institutes and industry complain about the limited knowledge and practical skills of graduates of the vocational schools. Problems of the schools are apart from old curricula and old teaching personnel the lack of labs to teach also practical skills. Another problem may be the low status of vocational training. The social status of a technician being trained at a vocational school is very low – according to interviewees – and so it is often intended to get a bachelor degree, who will work after the exam as a technician.

2.1.7 Framework conditions for research activities

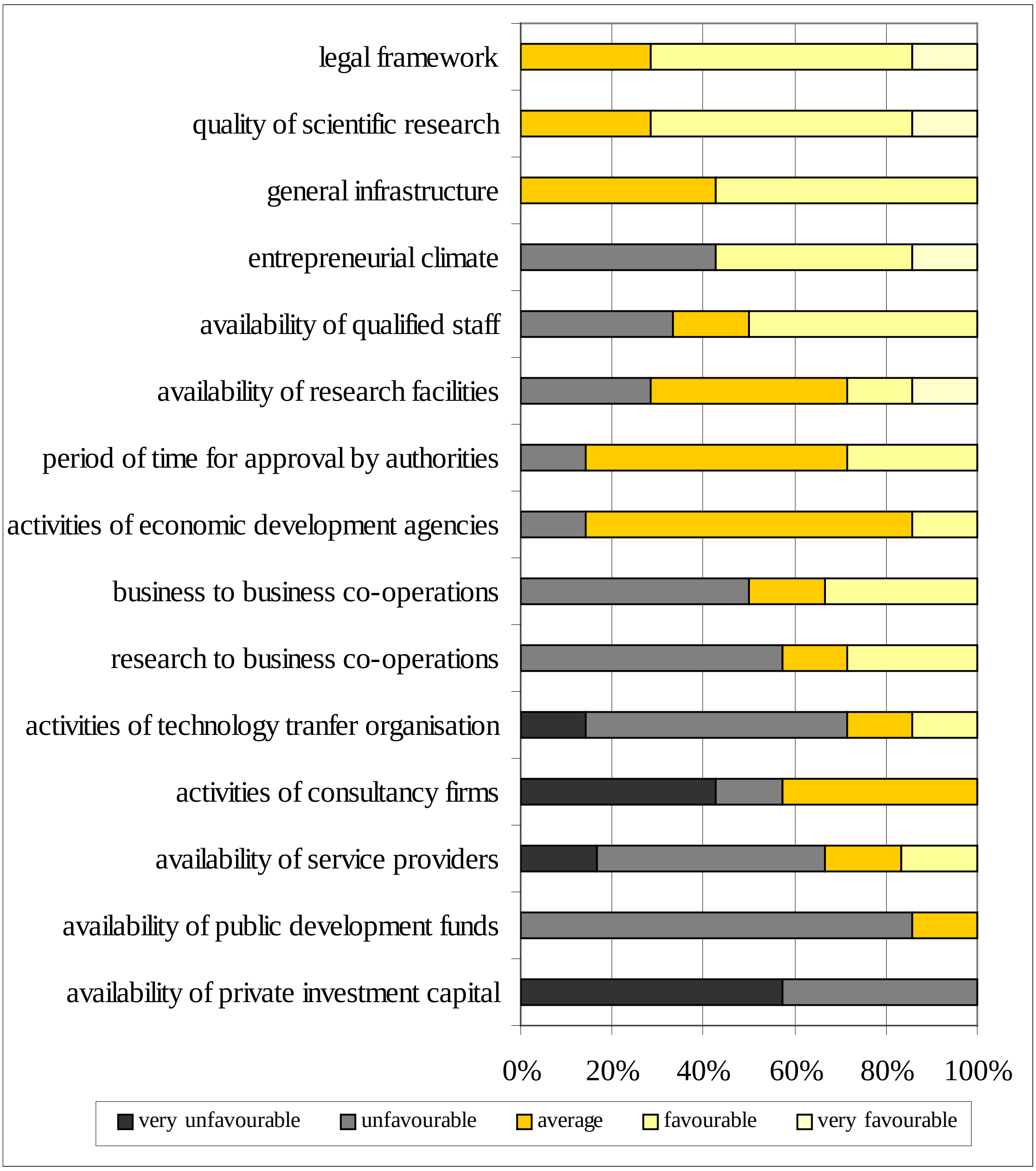
Good framework conditions are crucial for sustainable development of a sector. The biotechnology-related research institutions were asked to assess various aspects of framework conditions. The picture revealed both very positive conditions such as the legal framework and major hindrances, which pertain mainly the financing of research and business activities. Figure 2.12 summarises the results.

Nearly all interviewees were content with the legal framework in Estonia. There are often the same regulations as in the EU, still they are very unbureaucratic and are applied user-friendly. Other positive aspects of framework conditions were the availability of qualified staff, the general infrastructure and the entrepreneurial climate. Latter was due to the favourable tax regulation, low bureaucracy while company founding and the liberal economic policy of the government.

The activities of service providers and consultancy firms were assessed less favourable. Reasons for this are both the lack of appropriate agencies and their poor functioning. Many interviewees pointed out, that the agencies did not provide the required detailed information but only basic support. The major problem of Estonian framework conditions was attributed to the financing situation. This refers to all aspects of financing such as the financing of applied research projects and private financing of company activities.

Quality of scientific research was assessed by the researchers themselves as very good. This might result from the fact that Estonian researchers have acquired a number of international funds and are members in many European research projects. However, as bibliometric analysis showed in an international comparison the scientific performance is less favourable in Estonia.

Figure 2.12: Assessment of framework conditions for commercial or research activities by research institutions



Source: Fraunhofer ISI 2002

2.2 Industry/supply network

Taking the Estonian economy in total, since the mid 1990s in Estonia a large number of new firms was created. This led also to a shift concerning the country's firm structure. While in 1992 40 % of all employees worked for large companies (>500 employees), this share decreased to only 16 % in 1995 (Kurik et al. 2002).

In Estonia we find 11 biotech companies (see table 2.5) if we apply a rather stringent definition following the criteria which are used by Ernst&Young for the delimitation of "Entrepreneurial Life Sciences Companies (ELISCOs)" (Ernst&Young 1998). If a less stringent definition is used, the number increases to 24 biotech companies. This means that the result of our investigation ranges in the frame provided by former studies, in which a range between 17 and 40 specialised biotech companies was found in Estonia (Scandinavian Care Consultants 2002, Tartu Biotechnology Park 2002). At present the 11 core biotech enterprises have about 145 employees. In total the 24 companies identified employ around 160 people. The total turnover amounts to about 50 million EEK.

Some of the biotech firms we find in Estonia today were founded before the mid 1990s and even before the country gained its independence in 1991. The first company was established as early as 1989, but the majority of the companies are less than three years old. Among the firms that we interviewed during our investigation (N=16[3]) four were founded in 2002 and 2001 only (see table 2.5 for the companies which we interviewed). In addition to the interviews we sent data sheets to the companies asking for information that provides us with an overview about firm characteristics e. g. staff numbers, turnover, co-operations. We received the filled-in data sheets from 14 firms.

3 Asper and Biodata are closely interrelated and were represented by the same person.

Table 2.5: Biotech companies in Estonia

				No. of employees				
Company	**Field of activity**	**Location**	**Founding year**	**1-2**	**3-4**	**5-9**	**>10**	**VC acquired**
Core biotech companies[1)]								
AS PROEKSPERT/BIOEKSPERT[2)]	Software development and consulting	Tallinn	1993				X	
Asper Biotech	Genotyping – service and products	Tartu	1999				X	X
BioData OÜ	Bioinformation services	Tartu			X			
CELECURE AS	Development of cancer drug	Tallinn	2002			X		
EGEEN INC.	Pharmacogenetic clinical trial support	Tartu	2001			X		X
FitBiotech	DNA vaccines and diagnostics	Tartu					X	
INBIO LTD.	Development of novel biotherapeutics for cancer	Tallinn	1999			X		
LabAs Ltd.	Production and purification of mono-and polyclonal antibodies	Tartu	1991			X		
PROSYNTEST Ltd.	Production of active pharmaceutical ingredients	Tallinn	1989				X	
Quattromed LTD	Providing analytical lab systems and services	Tartu	1999				X	
Visgenyx Ltd.	Service for production of knock-out animals	Tartu	1999			X		

Table 2.5 continued

				No. of employees				
Company	**Field of activity**	**Location**	**Founding year**	**1-2**	**3-4**	**5-9**	**>10**	**VC acquired**
Extended biotech companies								
Applied Phenomics LLC	Platform technologies	Tartu	2002		X			
AS Kevelt	Medical diagnostics and chromatographic carriers	Tallinn						
Bignose AS		Tallinn						
CDN Ltd.	Production of labelled cell material, biofermentation	Tallinn	1994	X				
Estbioteh OÜ		Tartu	2001			X		
IASGEN OÜ	DNA amplification	Tartu	2000	X				
Immuntron OÜ		Tartu			X			
Lumifor		Tartu		X				
Naxo Ltd.	Molecularbiology for medical diagnostics	Tartu	1997		X			
OÜ Mikrotaim	Micropropagation of 7 different types of plants	Räpina	2001	X				
SOLIS BIODYNE OÜ	Production of thermostable DNA polymerase	Tartu	1996		X			
TorroSen OÜ	Commercialising the new technology of biosensors	Tartu	1999		X			
Vulpes AS		Tallinn						

1) Here we attempted to define core biotech companies in accordance with the definition used by Ernst & Young for Entrepreneurial Life Sciences Companies (ELISCO)
2) Those firms highlighted were interviewed during the project.

Source: Investigation of Fraunhofer ISI 2002

2.2.1 Areas of activity and competencies of Estonian biotech firms

Tartu and Tallinn are the two centres were the majority of the biotech firms are located. Most of the companies were created by researchers from one of the academic institutions engaged in biotechnology research in those cities (see chapter 2.1). Biotechnology is for most of the firms the major or even the only field of activity, which means that in most firms biotechnology contributes with about 75 % to 100 % to the firms' annual turnover.

The companies are engaged in biotechnology in various sectors, pharmaceutical and chemicals as well as the service sector being the most important ones. Thus, the development of new products or processes as well as providing services relating to diagnostics and therapeutics are the main field of activity of Estonian biotech firms. More than half of the firms that returned the data sheet are active in this sub-field. Almost as important is the sub-field bioinstruments. Other areas of activity are the development of bioprocess technologies and platform technologies or providing services related to those areas. However, less firms are actively involved in these areas. Only marginal commercial activities exist in the sub-fields of animal and plant biotechnology.

The vast majority of those biotech firms that returned the data sheet carries out R&D in their area of activity. 13 out of 14 firms mentioned R&D among the firms activities. However, the intensity with which R&D is carried out varies between the companies. R&D intensity, measured as the proportion of the R&D expenditures of the overall turnover lies between 1 % and 100 % in those firms. Concerning the employees engaged in R&D no general pattern of development can be found. Some firms increased the proportion of people engaged in R&D, while in other firms their share was decreasing between 2000 and 2001. In all cases this decrease identified was related to an increasing number of employees in total while the number of people carrying out R&D remained constant. Decreasing absolute numbers of R&D personnel was not stated by any of the firms interviewed. This points to the fact that firms extend their activities also in other areas than R&D. According to the data we gathered for personnel involved in manufacturing, staff numbers remained rather constant in most firms in that area. Manufacturing and marketing, however, is pursued by only about half of the firms interviewed.

Thus, manufacturing is still at its early stage in most Estonian biotech firms. This is also confirmed when the competencies provided by the firms are looked at (table 2.6).

In our data sheet we asked the firms to name their methodological or technological competencies. According to this self-evaluation (see table 2.6) more than two thirds of the firms do have competencies in gene amplification technologies (PCR). Cloning techniques and electrophoresis of proteins are also skills offered by a number of Estonian biotech firms. Bioinformatics, electrophoresis of DNA/RNA and purification of DNA/RNA belong to the competencies offered by more than one third of the firms.

Molecular biotechnology approaches which are related to the handling, characterisation and sequencing of DNA (and/or RNA) are intensively followed by Estonian biotech companies. In addition, a variety of tools used to analyse proteins are offered while technologies needed for functional genomics and proteomics are less dispersed as are bioprocessing techniques. The minor focus on bioprocessing points to the fact that Estonian biotech firms are still at a rather early stage of developing new biotech products for manufacturing, which at the same time is confirmed by the low number of firms that are actually engaged in manufacturing. The focus of Estonian biotech firms is at present directed towards analytics. In particular structural analytics is performed while functional analytics is of less importance.

Further more, concerning the business functions that are present in the firms only slightly more than a third say that they have a general management. Also in the interviews it became obvious that most firms lack management skills. In most cases, and especially in the very small firms, the scientists are at the same time responsible for the management of the firm and also the marketing of the products or services they offer. According to our data less than one third of the firms have a trained economist among their staff. Usually financial constraints prevent the firms from hiring people with management skills. In addition, a shortage of specialists with management skills and experiences was repeatedly mentioned, in particular managers who have additional knowledge in the biotech area are hardly available in Estonia. In the interviews it was mentioned that not having people with management skills is an important drawback, which can – in the worst case – even endanger the existence of the firm.

Generally, there is no clear division of labour in most firms, people working in those firms are engaged in all kinds of activities that are required to run the business ranging from R&D over manufacturing to marketing and management. For this reason it is also hard to differentiate shares of personnel devoted to various activities clearly. Furthermore, in particular for the very small firms it was found that their founders still hold double engagements as they often still are employed by the university or research institutes, and thus can devote only part of their working capacity to their business.

Table 2.6: Technical competencies available in Estonian biotech firms (N=14)

Technology competency	**No. of firms**
Gene amplification, PCR	10
Cloning techniques	6
Electrophoresis of proteins	6
Bioinformatics	5
Electrophoresis of DNA/RNA	5
Purification/separation of DNA/RNA	5
Biochemicals for biotechnology	4
Cell culture	4
DNA probes	4
DNA sequencing	4
Model animals (tests, trials)	4
Purification/separation of proteins	4
Recomb. DNA (incl. antisense, express. enhancement)	4
Cell fusion	3
Combinatorial chemistry	3
DNA/RNA micro-arrays	3
Mass spectroscopy	3
Tissue culture	3
Cell handling	2
Chiral synthesis	2
Enzymes for biotechnology	2
Fermentation technology	2
Functional genomics	2
Protein engineering	2
Protein synthesis	2
Other	2
Bioprocessing technologies	1
Cell therapy	1
DNA/RNA synthesis	1
Enzyme technology	1
Gene therapy	1
High throughput screening	1
Metabolic engineering	1
Micromanipulation	1
Micropropagation	1
Monoclonal antibodies	1
NMR spectroscopy	1
Proteomics	1
Purification/separation of other bio-molecules	1
Tissue engineering	1

Source: Fraunhofer ISI 2002

2.2.2 Firm Size

In Estonia most of the industrial and service companies are small-sized enterprises[4] (3-50 employees). According to the recently published report on "Innovation in Estonian Enterprises 1998 to 2000" (Kurik et al. 2002) about 82 % of all firms fall into this size group. About 15 % are medium sized (50 to 249 employees) and only about 3 % are large companies (>250 employees). The majority of the biotech firms belong to the group of small sized enterprises as well. Most of them have still less than 10 employees (table 2.7). However, taking staff numbers most firms grew during the years of their existence, while the extent of the growth varies between firms. Asper Biotech was the company that grew most significantly. It has now 35 employees while it had 5 employees when the firm was founded in 1999 (Moser Jones 2001). Quattromed is the second biotech company that has increased staff numbers significantly since its founding year 1999. Starting with five people now 22 people are employed by Quattromed (Quattromed 2002). The two other comparably large biotech companies Prosyntest Ltd. and AS Proekspert were established rather early, in 1989 and 1993, respectively. Both also increased their staff numbers but at a lower rate than those firms that were newly established since about 1999.

Table 2.7: Biotech firms by size[5]

No. of employees	1999 (N=8)	2000 (N=9)	2001 (N=10)	2002[1)] (N=10)
1-2	4	2	2	4
3-4	-	1	2	6
5-9	2	3	2	6
>10	2	3	4	5

1) Data generated based on interviews and data provided by Internet appearances of the firms.

Source: Fraunhofer ISI 2002

Most other biotech firms are still very small, even though the number of staff increased in recent years. But with the existing arrangements of sharing work capacities between the business and the academic institutions, even for the owners

4 For the community innovation survey (CIS) a distinction was made between small-sized companies (10-49 employees), which were included in the main CIS analysis and micro-enterprises (3-9 employees), for which a separate analysis was carried out. Here we used the data on both, small-sized companies and micro-enterprises.

5 Sizes were defined according to the definitions used in the special survey on small enterprises (3-9 employees) within the report "Innovation in Estonian Enterprises 1998-2000" (Kurik et al. 2002, p. 27)

of the enterprises, the growth potential of a significant part of the biotech companies is rather limited and often significant growth is also not intended by the owners. The majority of the owners prefer to keep the firms to a size that is easy to control and that does not demand major investment. They prefer to extend their business based on the income generated by the firm. Most firms do not have a definite growth strategy and thus are bound to stay close to their recent size.

The distribution of turnover by biotech companies is shown in table 2.8. This again indicates the small-sized character of most biotech companies in Estonia since only few companies have annual sales exceeding 5 million EEK. In addition, the growing character of at least some of the Estonian biotech companies can be illustrated by this table since several companies are moving in the group with more than 5 million EEK annual turnover in 2001 (table 2.8). For the eight companies for which sales figures were available for the years 1999 to 2001 a strong increase in the annual turnover can be registered for this time period: while in 1999 the average turnover amounted to 2.4 million EEK this figure rose to 4.9 million EEK in 2001 (this equals to a total growth rate of 104 % from 1999 to 2001). Most firms increased their annual turnover steadily since they have been founded. Some of them doubled or almost doubled their annual turnover between the years 2000 and 2001. According to the firms in 2001 about half[6] of them generated profits while about 20 % had to face losses.

Table 2.8: Turnover of biotech companies

Turnover per year[1)]	**1999 (N=8)**	**2000 (N=8)**	**2001 (N=16)**
below 1 million EEK	5	1	4
1 - 2.9 million EEK	-	2	5
3 - 4.9 million EEK	2	3	3
5 - 6.9 million EEK	-	1	2
7 - 8.9 million EEK	-	-	1
more than 9 million EEK	1	1	1
1) Data based on interviews and information provided in the data sheets			

Source: Fraunhofer ISI 2002

Although most of the Estonian biotech companies have only a small number of employees so far, most of them try to generate turnover by selling often standard

6 N=14, three firms did not give details on their financial situation in 2001.

type biotech-related products or services, also in the early stages of a company. In this respect the standard "business model" of Estonian biotech companies differs significantly from that of a lot of biotech companies in the USA and EU countries. This difference can be explained by the lack of (seed) venture capital in Estonia (see chapter 2.2.3), which does not allow to develop a company for a few years without achieving a substantial cash-flow within the company. In addition, it should be taken into account that most of the Estonian biotech companies do not fulfil the prerequisites to acquire substantial amounts of venture capital currently, so that revenues are often the main source of company financing during the start-up phase.

Estonian biotech firms are independent firms. So far Quattromed, a spin-off company from Tartu University that was founded in 1999, is the only company that sold shares to another enterprise. FIT Biotech, a Finnish biotech company that since 2001 also runs R&D facilities in Estonia, acquired 22.4 % of the shares of Quattromed. FIT Biotech also has the option to obtain the remaining shares of Quattromed, up to 100 %, until 2006 (FIT Biotech 2002).

2.2.3 Financing

The majority of the companies was founded using private resources of the people involved. Especially in the early years public funding was hardly available and thus founders had to rely on their own resources. In some cases loans were provided by ESTAG, which are, however, strictly project oriented and cannot be used for capital spending. One firm used funds from the Estonian Regional Development Foundation (ERDA), which is a subunit of Enterprise Estonia. ERDA has a start-up aid programme that provides up to 75 %[7] of the costs of investment required for setting up the business, while at least 25 % have to come from private resources of the founders. The maximum amount that can be received from ERDA is 100,000 EEK (Estonian Regional Development Agency 2002).

Due to the small size of most Estonian biotech companies, the investments used in the founding period were rather low. People mostly preferred to use their own money instead of applying for loans from either ESTAG or commercial banks. More than half of the companies said (table 2.9) that own capital was their most important source to finance their business activities. An even more important source is the turnover generated by the firms themselves. Public funds for R&D activities or public credit programmes play a secondary role so far.

7 At the time the biotech company was founded the rules were different, only 50 % of the investment costs were taken over by ERDA, the remaining 50 % had to be self-financed.

Table 2.9: Main source of financing business activities of Estonian biotech firms

Source of financing	**No. of firms**
Own turnover	10
Own capital	8
Venture capital	3
Public funds for R&D	2
Public credit programmes	1
Commercial credits	1
Others	1

Source: Fraunhofer ISI 2002

The availability of venture capital for small biotech companies is rather the exception than the rule in Estonia. Venture capital is available in Estonia primarily from international funds. Most of the venture capital spent on high-tech companies goes to the IT-sector. However, generally venture capital is rather spent on low-risk projects with a rather short-term return of investment instead in biotechnology (Tartu Science Park 2001) which often is regarded as high-risk business. According to the assessment of most interviewees the small size of biotechnology firms is hindering investments, too. In addition, venture companies active in Estonia do not have knowledge and experience in the area of biotechnology and thus, are in particular hesitant to invest in this sector. Often unrealistic expectations concerning time frame for the return of investment appear by potential investors.

So far only two Estonian biotech firms, Asper Biotech Ltd. and EGeen, were able to attract venture capital. Given the recent size and modes of operation of many of the biotech companies (see chapter 2.2.1) it does not seem very likely that venture capital can be attracted by many of them. So far only very few Estonian biotech companies have filed a national or international patent or are in the process of applying for a patent (see chapter 2.2.6). Among those companies which practise an active patenting and IPR policy is Asper Biotech Ltd. EGeen has not applied for a patent itself mainly due to the short life span of the company[8]. However, some of the founders of EGeen are among those Estonian persons who filed international patents in the biotech field in recent years. In general, venture capital companies regard a strong patent portfolio and an active IPR policy as one of the main prerequisites to invest in a biotech company. Therefore, it seems necessary that the great majority of the Estonian biotech companies change their IPR and patenting strategy in the coming years, in order to be able to attract venture capital either from domestic or international sources.

8 The company was founded in 2001.

EGeen is a Tartu- and Boston-based biotech firm that was founded in the context of the Estonian Genome Project (see chapter 2.1.1). At present the major task of EGeen is to attract investors for setting up and exploiting the database that is being generated within the Estonian Genome Project. EGeen is the "exclusive licensee, business unit and commercialisation arm" (EGeen 2002) of the Estonian Genome Project. The aim is to develop EGeen towards a biopharmaceutical company that uses health, genomics and proteomics data, which will be gained from the Estonian Genome Project, in order to develop pharmaceutical and health-care products. In particular the development of individualised medical solutions will be aimed at. So far, EGeen was able to attract around 71 million EEK in a first venture capital round. Estonian and international venture capital funds invested in EGeen. Among them are Draper Fisher Jurvetson ePlanet Ventures (DFJ ePlanet), two funds from the Small Enterprise Assistance Fund (SEAF), SEAF CEE Growth Fund and The Baltics Small Equity Fund. Furthermore, Biobank Technology Ventures provided investment for EGeen. A second venture capital round will follow almost immediately as the recent situation at the international venture capital markets is rather difficult for biotech companies. Another important task of EGeen is to look for partners for collaboration which are able to validate drug target candidates and genetic drug profiles (EGeen 2002).

Asper Biotech is the second Estonian biotech company that was able to attract venture capital so far. Asper Biotech is a company that provides genotyping services and develops assays and biochips for high-throughput genotyping for diagnostic purposes and personalised treatment of diseases (Asper Biotech 2002). In two venture capital rounds Asper was able to raise 18 million EEK from the Small Enterprise Assistance Fund and a follow-up fund thereof. In 2003 another venture capital round will be started seeking another 90 million EEK (Moser Jones 2001). Additional funds are required in order to expand business activities of the company.

As mentioned above (see chapter 2.2.2) *Quattromed* raised money by selling 22.4 % of the firm shares to a Finnish biotech company that – FIT Biotech – since 2001 also operates in Estonia. Quattromed itself has two areas of activities. On the one hand, it provides services in molecular diagnostics to, primarily, Estonian medical institutions like hospitals and surgeries. On the other hand, Quattromed is engaged in functional genomics and proteomics, developing test kits for the characterisation of proteins. This activity is mainly directed towards international clients (Quattromed 2002). The ownership of parts of Quattromed by FIT Biotech does not seem to influence the independency of Quattromed significantly so far. At least no hints were given during the interviews in this respect.

In order to finance R&D activities, very few biotech firms also applied for funding from the European Commission e. g. within the framework of the CRAFT Programme. Consortia were organised with academic institutions and other companies. The application procedure appeared to be more difficult than expected.

Based on the experiences made it was acknowledged that in the future external support would be needed and asked for in the process of writing proposals. In Estonia there are a few agencies offering this kind of support. One example is Innopolis, a firm that successfully provides consultancy and assistance for applications for EC funding.

The equipment required for setting up the business of a biotech company was organised in different ways. In some cases the firms are still operating within the university environment and thus can access university facilities on a contract basis. Other firms started off renting the laboratory equipment required. Another firm received, based on individual contacts, second hand laboratory equipment without any costs.

As shown in the upper paragraph Estonian biotech companies try to organise their equipment in cost saving ways in order to spare the rare financial resources. The same applies to consumables which are rarely purchased from external sources, but in-house solutions are preferred which save financial liquidity. Estonian research institutions react in a similar way with regard to consumables. Related to the purchase of equipment most research institutes complained about the very limited public financial resources for this purpose, which in consequence leads to strategies to organise the most important parts of the required equipment in "budget-saving" ways (e. g. by buying used equipment in Finland or other countries). In case external sources (e. g. EU, specific charities, foreign governments) provide financing for the purchase of new scientific equipment, Estonian research institutions buy it internationally, not least due to lack of such an industry in Estonia. Related to clinical trials, in which considerable amounts of consumables are needed, several interviewees stated that potential Estonian suppliers often do not meet the GMP or other requirements asked for by the pharmaceutical companies carrying out such trials, so that the respective consumables are bought from international companies.

2.2.4 Markets

Estonian biotech companies are primarily export oriented. Eleven of the biotech companies which filled in the data sheet provided information related to exporting of biotechnology-related products or services. As shown in figure 2.13 around three quarters of those companies generated a turnover of less than 3 million EEK by exporting biotechnology-related products or services in 2001. Two companies exported biotech-related goods worth between 5 and 6.9 million EEK in 2001 (figure 2.13). With respect to the proportion of sales which are generated by exporting biotech products and services, a rather heterogeneous picture emerges since on the one hand around half of the companies have an export share of less than 20 %, while on the other hand almost the same number of companies achieved more than two thirds of their turnover outside Estonia (table 2.10). In both groups companies are included with relatively low total turnover of less than 3 million EEK, but also companies with the double figure in 2001.

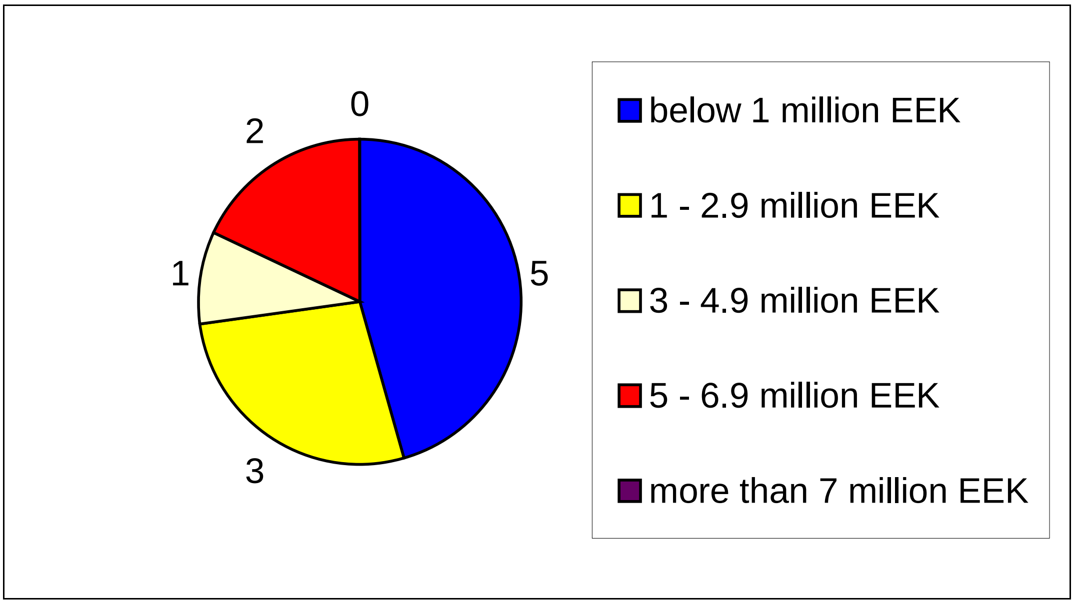
Table 2.10: Proportion of exports of biotech products or services in 2001

Proportion of exports	**Number of companies**
Below 20 %	5
21 % - 40 %	1
41 % - 60 %	1
61 % - 80 %	2
More than 80 %	2

Source: Fraunhofer ISI 2002

Most of the Estonian biotech companies are at least partly export oriented because the market for biotech companies within Estonia itself is very limited as there is hardly any demand for biotech products and services within the country at present. Potential application industries like the food processing industry, chemical industry or environmental technology firms do hardly use any products or services offered by biotech companies. In addition, in particular the pharmaceutical sector is missing almost entirely in Estonia, while most biotech firms are focusing on diagnostics and therapeutics. One exception is Quattromed, the company generates about half of its income within Estonia through the diagnostic services provided to hospitals and surgeries. Apart from that academic institutions and other biotech companies are basically the only existing clients for biotech firms within Estonia.

Figure 2.13: Turnover generated by exports of bioech products or services in 2001



Source: Fraunhofer ISI 2002

Expectations concerning increasing internal demand are related to the Estonian Genome Project. According to the Estonian Human Genes Research Act the samples drawn from patients within the framework of the project have to be analysed within Estonia, which could open market opportunities for firms focusing on this segment, which is at present only Asper Biotech. However, an open call for tender will be released for the genotyping activities. The call will be open for national and international firms. In order to win the project, non-Estonian firms would have to set up the facilities needed to perform the analysis within Estonia in order to comply with the rules defined by the Human Genes Research Act. Alternatively, collaborations with Estonian firms would be an option.

So far, Europe and the USA are the major markets for Estonian biotech firms. The recently difficult situation of the biotechnology sector internationally influences Estonian biotech companies, too. This relates in particular to biopharmaceuticals where international competition seems to increase in the last few years. On the one hand pharmaceutical companies increasingly arrange close partnerships with leading biotech companies in relevant fields of drug discovery and drug development, on the other hand there is a tendency to arrange such co-operation agreements as flexible as possible in order to be able to switch to another technology option (and another co-operation partner) if required. This means that biotech companies often first have to show their expertise and ability to carry out such co-operation projects on a relatively limited scale before pharmaceutical companies are willing to enter in a wide-ranging partnership. Related to the

Estonian research institutions and companies this implies that they are competing with the world-wide leading institutions in a specific area if partnerships with big pharmaceutical companies are concerned. There might be better opportunities to arrange co-operations with medium-sized pharmaceutical or biotech companies which often look for more cost-effective solutions so that the advantages in salaries paid in Estonia might come into force in this group to a higher extent.

An idea mentioned by a number of representatives of biotech firms is to develop a national market for biotech products by developing the Estonian biotech industry. The growing number of firms and the growth of the firms themselves would generate demand for biotech products and services inside the country, and thus a national market would develop. However, the problem underlying this idea is that right now many companies do not have an explicit growth strategy. They prefer to remain at their recent level or grow rather incrementally in order to minimise their own financial risk. This behaviour significantly limits the growth potential of the entire sector and has direct consequences for the demand potential of other biotech companies.

A major drawback is that in most Estonian biotech firms clearly defined marketing strategies are missing. Firms often rely on very few customers. Often company-customer relations are based upon individual contacts between firm owners, in particular in the case of the very small biotech companies and customers only.

The way company-customer relationships are organised is in many firms one reason for the negligence of marketing aspects. The capacities of many companies are exploited by the existing relationships. The limited interest for growth, that was expressed by many interviewees, seems to prevent to actively market the company and the offered products or services to a broader clientele. This would be necessary not only to open the chances for further growth but also to avoid existential threads in case an important customer is lost. In addition, most firms are lacking specific management and marketing know-how which has a negative impact on the awareness that specific efforts are needed to build up a distinctive marketing strategy and to extent the customer basis. In many cases the existence of an Internet presence of the biotech firm was mentioned as the only way to present the company and sell the products or services offered. However, some interviewees requested concerted actions by the Estonian actors in biotechnology, which need not necessarily to be limited to companies but should include research institutions as well, to make their activities internationally known. Common appearances at international trade fair and exhibitions were suggested, which could reduce the costs for being present at respective events for the individual firms at the same time.

2.2.5 Availability of staff

Firms expressed differing views concerning their difficulties to recruit required staff, depending on what kind of staff was concerned. Quite unanimous was the assessment concerning the lack of people with management skills, in particular people that combine scientific knowledge and management skills are hardly available in Estonia. Recruiting experienced biotech managers internationally was regarded as difficult as well due to financial reasons and language problems.

The availability of scientists was not mentioned as a major constraint. The vast majority of the firms, about 80 %, said that they are able to recruit graduates and postgraduates with knowledge and skills in biotechnology. One reason for this rather positive assessment is the fact that biotech firms often pay higher wages than academic institutions, and thus scientists are rather interested in working for companies. As a rule, the scientists are well trained even though they have not necessarily all the skills and knowledge of biotechnological methods required by the firms, which makes training on the job indispensable. However, some firms judge the necessity to continuously train their staff rather as a burden while other firms are better prepared to provide the respective training. In very few cases biotech companies provide practical training to students, offering a possibility to improve the practical skills that are required by the firms already at an early stage.

More than two thirds of the firms mentioned the Tartu University as the institution the graduates they employ come from, one third referred to Tallinn Technical University.

In general, the availability of technicians is more problematic than that of scientists. Often graduates holding a bachelor degree are employed as technicians as there are very few institutions were technicians are trained. Only recently a new curricula for technicians was introduced at the Räpina Horticultural College, which was defined in collaboration with the Tartu University. The first group of eleven technicians will finish their training in 2003. A second group of 15 students started in 2002. Thus, so far there are no practical experiences by the firms concerning the quality of the training provided. At present the problem in Räpina is the lack of laboratory facilities to provide the required practical training. So far the problem is solved by using facilities at the Tartu University.

2.2.6 Patenting

Patenting is not the most important way to protect new products or services which is used by Estonian companies (table 2.11), e. g. only around 4 % of the manufacturing or service companies participating in the CIS survey applied for a patent between 1998 and 2000 (Kurik et al. 2002). They rather use the lead time advantage on competitors to protect their products or services, which is followed by the registration of trademarks. Obvious is the difference of the significance of patenting depending on the firm size. Large companies much more often use patenting to protect their products than do small companies. The analysis of patent applications that we performed (see annex A3) confirms this, too. Very few Estonian patent application in general and also in biotechnology were identified. Furthermore, most of the patents were applied for by foreign institutions while the inventors were Estonian.

Since July 1, 2002, Estonia is a member of the European Patent Organisation. Before Estonia became a full member of the European Patent Organisation Estonian institutions were granted special conditions concerning patenting fees. They had to pay a reduced fee which was only 25 % of the regular costs. Now Estonian institutions have to cover full costs, e. g. the costs for patent searches and examination procedure increased from 20,000 EEK to 60,000 EEK.

Table 2.11: Protection methods of IPR by sector and number of employees, between 1998 and 2000 (in % of all companies responding in the CIS survey)

Protection method	**Manu-facturing**	**Services**	**10-49 employees**	**250+ employees**
Patents				
Applications	4.3	3.8	3.1	13.7
Granted	6.1	5.1	4.8	17.2
Design Patterns	2.2	1.2	1.4	6.7
Trademarks	15.0	14.0	11.8	33.1
Copyrights	2.8	3.2	2.4	6.1
Secrecy	12.8	11.7	10.7	22.0
Complexity of design	11.8	8.6	9.4	15.2
Lead time advantage	23.5	20.4	20.3	28.2

Source: Kurik et al. 2002

In general, biotech firms do not have their own specialists familiar with the rules and requirements concerning Intellectual Property Rights (IPR). Often the awareness of the relevance of patent protection is not well developed, neither at the firm level or the research institutions nor at the level of public agencies. Firms need to develop an understanding concerning the fact that building up a patent portfolio is necessary to improve the attractivity of Estonian biotech companies for investors. The biotech firms we interviewed generally acknowledged the importance of patent applications to protect products and processes. Financial constraints were mentioned as the main obstacle that prevents firms from applying for patent protection so far. Attempting patent protection is hardly funded by public agencies. Compared to other sectors biotech firms seem to pursue patent applications till the final phases, which are the most cost intensive, more frequently. As the majority of the biotech firms are primarily export oriented, international patent applications are more relevant than national ones. External support is needed in order to realise in particular those patent applications. The Estonian Patent Act, which came into force in 1994, was formulated following the regulation of the European Patent Convention. Preparing the accession to the European Patent Convention further harmonisation was realised.

A couple of commercial agencies or firms provide support and consultancy on IPR, like e. g. Käosaar, Lasvet and Ustervall. *Käosaar* is one of the biggest patent and trademark agencies in Estonia with branches in Tartu, Tallinn and Pärnu. One of the main areas of activity of Käosaar lies in the pharmaceutical sector. However, the most important task for Estonian patent and trademark agencies is at present the realisation of patent and trademark applications of foreign firms at the Estonian Patent Office. The services offered by the patent agencies include preliminary searches for patents that would possibly prevent Estonian firms to protect their own inventions up to actually seeking patent protection, which includes the formulation of the patent applications. In order to apply for patents in foreign countries, collaborations exist with patent firms in the respective countries. Most important for Estonian biotech firms are the USA, Europe, Australia and China. Due to the increasing patenting costs depending on the number of countries patent protection is attempted for, Estonian biotech companies limit themselves to their most important markets.

Departments dealing with IPR exist also at the universities, but at present the universities face the problem of recruiting experienced staff in this area. Again one of the reasons is the fact that commercial enterprises are paying higher wages or people founding their own business providing IPR-related consultancies commercially and experts are in short supply. As a consequence, the Tartu University for instance released a call for tender concerning the provision of consultancies on IPR, which includes national and international patent protection and trademarks. At the Tallinn Technical University the R&D Department, which is financed by the SPINNO-Initiative, provides support relating to IPR to the researchers. The department employs one patenting specialist, in addition, external support is used for preparing patent applications.

Differences exist between the Tartu University and the Tallinn Technical University concerning the ownership of the invention and the resulting patent application. In Tartu the university owns the patent right. The inventor should receive a "fair share" of the income generated from the patents. In Tallinn the situation is less clear. For each patent an agreement between the university and the inventor has to be reached concerning patent ownership. Patent applications are, however, not financed by the SPINNO-Initiative. At present Tallinn Technical University evaluates the possibility of setting up a special foundation for financing future patenting activities.

2.2.7 Co-operation activities

Seven of 15 biotech enterprises that participated in the written survey report at least one co-operation partnership of any kind. Compared to data from the CIS-Report (Kurik et al. 2002), where a rate of around 30 % to 40 % for all manufacturing companies is described for the years 1998 to 2000, this is a slight improvement, but still some of the interview partners assessed co-operation or external sources of information as not very relevant to acquire knowledge for the company. One of the companies highlighted the importance of co-operation for the implementation of clinical trials and to gain information about fields in which the company has no own expertise.

Four of 13 companies gave a 'very unfavourable' or 'unfavourable' evaluation of the business-to-business co-operation, eight assessed it as 'average', only one gave a 'very favourable' assessment. The assessment of research-to-business co-operation was quite similar, nine had a '(very) unfavourable' assessment, only one called this aspect 'very favourable'. This might correlate with the availability of research facilities, which was assessed as 'unfavourable' by most of the companies as well.

The not very positive evaluation of the framework conditions relating to co-operation aspects might in part result from a perceived low effectiveness of the respective support by public programmes. To find a partner was called a matter of luck by one interviewee, several called the official ways (e. g. technology transfer or partnering programmes, fairs) ineffective and too complicated. Personal contacts seem to be very important to establish co-operation partnerships for the firms. Additional problems for the companies are unsatisfactory offerings by the universities: high levels of bureaucracy at the universities result in the fact that university professors in part like more to work on the basis of private contracts than officially for the university. Other companies report good collaboration activities with Estonian universities which comprise the common use of resources as laboratory devices, transfer of knowledge and licensing of procedures that were developed at the university.

Co-operation partners

Most of the co-operation partners of the companies are SMEs (18 of 50 co-operation relationships) and research institutions (17 relationships), only two co-operate with large firms, 13 co-operations exist to other institutions. The majority of co-operations commenced in the year 1999, only eight before this date beginning in 1989. Between seven and eleven new relationships of the companies to other organisations began in the last three years.

Most of the co-operation partners are settled in Tallinn or Tartu regions (15 and 16 partners, respectively), one in the rest of Estonia. 16 co-operation partners come from foreign countries. The states of the foreign co-operation partners are listed in table 2.12. This shows rather intensive co-operation activities of Estonian biotech companies to Scandinavian and other EU countries, while the USA and in particular other countries outside Europe are of low relevance (table 2.12).

Table 2.12: Origin of foreign co-operation partners of companies

Country	**Frequency**
Finland	4
Finland	4
Germany	2
Germany	2
Sweden	2
Sweden	2
USA	2
USA	2
France	1
France	1
Italy	1
Italy	1
Korea	1
Korea	1
Lithuania	1
Lithuania	1
Netherlands	1
Netherlands	1
United Kingdom	1
United Kingdom	1

Source: Fraunhofer ISI 2002

In 1998 to 2000, most of the co-operation partners of the Estonian industry also came from Estonia itself, followed by the EU inclusive Iceland, Norway, Switzerland and Liechtenstein and to a smaller extend also from EU candidate countries. The USA, Japan and other countries were less relevant for the Estonian industry (Kurik et al. 2002). In this respect, the countries to which co-operation partnerships exist are similar for biotech companies as for the Estonian industry in total.

The share of regional versus foreign contacts in our survey can be compared to a study of Fraunhofer ISI about the biotechnology innovation system in the region of Hanover, Germany in the year 2000 (Menrad et al. 2001). Around one half of the co-operation partners came from the region of the co-operating enterprise. The partners of the companies in the Hanover region were to around 40 % other enterprises, but 28 % were research institutions and 15 % institutions with financial or transfer services. This means that in the tendency, more of the Estonian biotech enterprises had collaborations with research institutes than the biotech companies in the Hanover region.

On the basis of the written survey the regional distribution of co-operation relationships in Estonia is given in table 2.13.

Table 2.13: Regional distribution of co-operation relationships of companies

		Origin of co-operation partner				**Sum**
		Tallinn	Tartu	Rest of Estonia	Outside Estonia	
Region of company	Tallinn	8	2		5	15
	Tartu	6	12		12	30
	Rest of Estonia	1	2	1		4
Sum		15	16	1	17	49

Multiple responses, k=49 co-operation relationships of n=10 companies

Multiple responses, k=49 co-operation relationships of n=10 companies

Source: Fraunhofer ISI 2002

The table shows that most of the co-operation partnerships of companies from Tallinn exist to partners in the same region, only two partnerships relate enterprises from Tallinn to institutions in Tartu. The same can be said for companies from Tartu, where co-operations exist mainly to partners in Tartu or in foreign countries.

A major problem of Estonian biotech companies seems to be the nearly total absence of co-operationships with large firms, mainly due to lack of such companies in potential application industries of biotechnology in Estonia. An additional problem represents the fact that single Estonian biotech companies heavily depend on single co-operation partners. This can result e. g. in the loss of a whole market in a country when the foreign co-operation partner became insolvent. One interviewee supposed that his enterprise was not interesting enough for large firms as a co-operation partner because of its small product portfolio.

Areas for co-operations

Table 2.14 gives an overview of the purposes for which co-operation relationships are used by the Estonian biotechnology companies. Because multiple responses were allowed, the percentages sum up to more than 100 %. More than one third of the companies use co-operations to solve scientific questions or to develop products, one third co-operates for contract manufacturing or clinical trials. Also important is the marketing or distribution of products, of lesser relevance are the financing of the company, questions of licensing or authorisation and business consultation. Other purposes for co-operation are, for example, data security, IT-solutions, quality control and legal questions.

Table 2.14: Purpose of co-operation relationships of companies

Purpose of co-operation	**% of companies**
Solving scientific questions	37.5
Product development	37.5
Contract manufacturing/ clinical trials	33.3
Marketing/distribution of products	20.8
Financing of the company	12.5
Questions of licensing/authorisation	12.5
Business consultation	12.5
Arrangement of co-operation partnerships	4.2
Other	6.3
k=48 co-operations of n=10 companies, m=85 responses	

Source: Fraunhofer ISI 2002

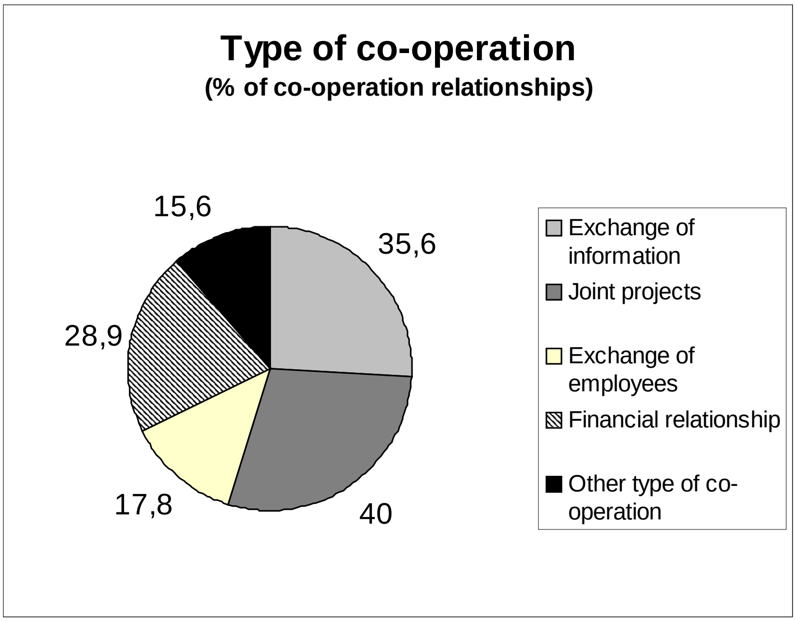
The spectrum of the collaboration purposes of the Estonian companies is also similar to the Hanover region, where scientific questions, the transformation of knowledge into products and contract manufacturing were also the most important purposes, followed by marketing and distribution of products (Menrad et al. 2001).

Type of co-operation activities

As figure 2.14 shows, the biotechnology companies which participated in the written survey have co-operations of various kinds: 40 % of their co-operations consist of joint projects, further important types are the exchange of information or financial relationships. To a smaller amount also the exchange of employees and other types of co-operation are carried out. This profile differs from the co-operation activities in the Hanover region especially in the fact that the Estonian companies have more partnerships with a financial background than the companies in the Hanover region (Menrad et al. 2001).

The form of the co-operation activities is mostly adopted to the specific conditions and aims. Very frequent are joint projects that can vary from counselling or joint publications to the establishment of large consortia. In some cases, no formal contract was set up between the co-operation partners. This can lead to problems, in part because from the companies' perspective university institutes are not used to the requirements of the business sector.

Figure 2.14: Type of co-operation of biotech companies



Multiple responses, k=45 co-operation relationships of n=10 companies

Source: Fraunhofer ISI 2002

Activities to improve co-operation

The interview partners from Estonian biotech companies proposed several actions to improve the framework conditions for national and international co-operation. These are

- A better functioning science park should bring together the high-tech enterprises. This should be supported by the state and not be financed by the science park's own earnings.

- Estonian companies should be made more internationally known, to this end the participation of Estonian companies at international fairs and conferences should be financially supported.
- In general, networking activities should be initiated, for example the organisation of fairs to give the opportunity for contacts to possible investors.
- As it is important for foreign partners to reach the Estonian companies more easily, attempts should be made for more direct international flight connections.

2.2.8 General initiatives to support biotech companies

There are a couple of new initiatives that are being set up or are in a planning phase in order to facilitate the founding of new firms or the running of existing ones, some of them only in the area of biotechnology, others with a broader focus. In addition, there are several initiatives running to re-organise or create science and technology parks, some with focus on biotechnology, others with a broader technology scope.

At the Tartu University the Tartu Institute of Technology, which is the successor of the Tartu University Centre of Technological Excellence, was founded in 2001. So far, the institute is still rather fiction and in its incubator phase with the business and the financial plan, pre-requisites for future financing, still in need to be approved by the Ministry of Economic Affairs and Communications. So far, the Tartu University provided a building to the Institute of Technology which will be renovated and should be ready by autumn 2003. According to interviewees it is planned that the university provides the funding for the renovation. Financing of the equipment needed for the facilities has been applied for at the Ministry of Economic Affairs and Communications within the framework of a SPINNO project. So far the project was not agreed from the Ministry (see chapter 2.3.2).

The aim of the Institute of Technology is to generate new ideas and technological solutions and to support the setting up of spin-off companies based on these ideas. The activities of the institute are organised in four areas, which are all relevant for the further development of biotechnology: materials and chemical technology, information technology, environmental technology and biomedical technology. Setting up the institute was also triggered by the fact that the original concept of the Centre of Technological Excellence, which was thought as a rather virtual institution with the aim of identifying research performed at the potential for commercialisation. However, it was recognised that so far there were hardly any marketable developments at the university, and thus it was decided that a facility was needed that would enable to carry out research from the rather early stages of the innovation process up to product development. To provide specific facilities that would bring together research groups working towards marketable products was estimated as a pre-requisite in order to develop also a new, innovation-oriented culture. The services the institute intends to provide to the different research groups and start-up companies are to support handling of IPR by a patenting and licensing unit and attracting resources from external sources either private or public. A task for the planned financial unit would be to find industrial partners that would be interested to commercially exploit research results produced by the groups working at the institute. The firms would receive the required licenses from the institute. In case industrial partners could not be found, the institute would support the establishment of a spin-off company. The institute would hold the major part of shares from those companies. Support would be provided for defining business plans and financing the company. Within three years the company needs to prove its sustainability. At that stage the institute would sell its shares and use the resources acquired for the support of new projects or companies. In addition to the patenting and licensing unit and the financial unit it is planned to set up a spin-off support unit, which would be responsible for parts of the above described activities, too. Furthermore, an education unit is planned that would provide and organise continuous education to the groups and firms belonging to the institute in various areas.

Incubation centres, science and technology parks

In Tartu and in Tallinn there are some already existing incubation centres or science and technology parks which can be used by biotech companies as well. In addition, there are several initiatives going on in this area in both cities.

Tartu Science Park which was founded in 1992 is the oldest and currently the only science park in Estonia. Since 1996 it operates as a non-profit foundation under private law and was established by Tartu City, Tartu County Government, Tartu University, Estonian Agricultural University and the Tartu University Institute of Physics. It has a management team of three to four persons (Scandinavian Care Consultants 2002) and hosts around 20 companies amongst them with Immunotron OÜ, Naxo and Solis Biodyne OÜ also three extended biotech companies (Tartu Science Park 2002). Most of the other companies concentrate on IT and materials, but it was estimated by interviewees that only half of the firms that are actually located in the Science Park are science- and technology-based companies. At present the Science Park provides only empty space to the firms but no equipment. The facilities are in a rather bad shape, which makes the Science Park not very attractive to the target group. According to interviewees' information the services offered by the Science Park are not clear and changing in a very short period of time. In addition, there are frequently re-organisation activities and management problems occurring in the Park which does not improve the situation and impede a sound mid-term strategy for the Park.

In addition to the Science Park, the Tartu Biotechnology Park was founded in Tartu in 2001. The biotech park is a private enterprise that was supported by ESTAG and co-financed by the Swedish government. Shareholders of the biotech park are the Scandinavian Care Holding, the Tartu Science Park Foundation, the Estonian Genome Project Foundation, EGeen, Quattromed, Asper Biotech, Immunotron, Visgenyx and Kaltec. Originally, a Swedish investor was prepared to build new facilities to be used by the biotech park. Due to financial problems of the investor this could not be realised and the timing and financing had to be changed. At present it is planned to have new facilities by 2005. Until than the biotech park occupies parts of the Tartu Science Park. It is intended to renovate facilities currently used by the Estonian Genome Project using a bank loan. In order to realise the building of the new facilities, private investors need to be found. At present the biotech park provides only empty space to the firms but no equipment. The facilities are in a rather bad shape, which makes the biotech park not very attractive to the target group and as there is no specific equipment provided by the park, there does not seem to be any additional incentive to set up a business within the biotech park. According to information given by some interviewees, it is intended that part of the business-related activities of the Estonian Genome Project are hosted in the renovated building of the biotech park.

Another initiative in the biotech field is the Biotechnology and Incubation Centre (BDIC), which is planned to be built in Tartu as part of the Estonian BioCentre. The aim of the BDIC is to provide the necessary technological infrastructure, facilities and services to set up start-up and spin-off companies in biotechnology, which should facilitate the transfer of results from basic research into industrial development (see also chapter 2.1.1). According to information given by the interviewees it is planned to finance the BDIC with the help of EU funds, so that it will take at least two years until the building will be realised and the incubation centre can start its activities.

Several interviewees criticised that there is no co-ordinated strategy for incubation and technology park services for biotech companies in Tartu. The impression arose that several institutions try to realise their own plans in this field instead of developing a co-ordinated and joint activity in order to efficiently use rare resources. In addition, it appears that the Tartu Institute of Technology and the BDIC have overlapping objectives and are at least partly aiming at the same clientele – which is relatively limited in numbers at present. The major difference is that the Institute of Technology will not only focus on biotechnology but will also cover materials and chemical technology, environmental technology and information technology. In addition, the Institute of Technology attempts to cover earlier stages of the innovation process as well. Altogether, it would rather be recommended to join forces instead of following too many separate initiatives in the Tartu area.

In Tallinn, it is planned to establish a new technology park by the Tallinn Technical University, the city of Tallinn and the Ministry of Economic Affairs and

Communications (ESTAG). For this purpose a specific foundation was created in which the state brought in the real estate property located in the area foreseen for the park. In a first phase the technology park priority is given to physics and IT since a lot of companies already exist in this field and are located nearby Tallinn Technical University. For these companies and some related research institutes it is foreseen to establish a new building with around 5,000 m^2 in the coming years using EU funds as well as financing provided by the founders of the technology park. In addition to renting buildings and rooms, the technology park intends to offer incubation services to start-up companies and company founders, as well as business development (like support for technology transfer, search for business partners and co-operation projects as well as financing) and marketing services (e. g. dissemination of business offers, participation in marketing networks, organisation of contact finding, public relation activities) to existing companies. In a second step of the technology park initiative it is planned to establish a new building for the newly created Faculty of Natural Sciences of Tallinn Technical University in which space for biotech companies as well as some shared-used laboratory space and specific equipment could be included. However, a business plan for these activities does not exist so far neither is financing clarified, so that currently no specific technology park exists for biotech companies in the Tallinn region.

On the area of the foreseen technology park in Tallinn there exists already a small incubator for technology-oriented firms which was established by the city of Tallinn in an existing building. Currently, around 350 m^2 space are available which are rented to a reduced price to start-up companies. It is foreseen to substantially increase the incubator capacity in Tallinn within the technology park initiative.

2.3 Finance/industrial development network

The financial and business development framework of biotechnology in Estonia is analysed in the following chapter. This includes the roles of private and public funding possibilities of biotech companies and research institutions in applied research, existing innovation support structures and services as well as the general framework for biotech and other companies provided e. g. by tax regulation or the social security system.

2.3.1 Private financing of biotech companies

Private financing of business activities was outlined as one of the major problems for biotech companies in Estonia both during the interviews and in the opinions expressed in the filled-in data sheets (see chapters 2.1.7, 2.2.3). In addition, the results of several studies analysing the Estonian innovation system in general or specific parts of it also stressed the crucial role of the financing system for innovations (e. g. Anonymous 2002, Scandinavian Care Consultants 2002, de Jager et al. 2001).

Currently the Estonian financial market is characterised by a low amount of venture capital. Although a survey of the Ministry of Economic Affairs and Communications estimated that ten venture capital companies conduct investment activities in the Baltic States and that around 1.5 billion EEK of venture capital are available in Estonia (Anonymous 2002), this result cannot be substantiated by our analysis. So far only two Estonian biotech firms, Asper Biotech Ltd. and EGeen, were able to attract a total of around 89 million EEK venture capital in recent two years (for details see chapter 2.2.3). From this sum around 42 million EEK were invested by one venture capital company (Small Enterprise Assistance Fund, SEAF) operating in Estonia (with two different funds: The Baltics Small Equity Fund and SEAF CEE Growth Fund), while the remaining 47 million EEK were provided by international venture capital companies. In this context it has to be taken into account that EGeen represents an international company with a location in Boston which facilitates acquiring venture capital on the US market.

Important criteria for selecting biotech companies to be invested in by venture capitalists are an innovative approach or technology (ideally protected by a strong patent portfolio on an international level), a convincing business concept, an experienced management team as well as a kind of "unique position" of the biotech company. In general, the investing venture capital companies give assistance to the biotech companies, in particular advice to enhance the management and economic capabilities of the biotech company (e. g. in marketing, financing). Often the venture capitalists bring in selected personnel (e. g. a CEO, CFO) in the biotech company or try to organise the company according to business needs. Additional support is given related to regulatory and IPR issues (in particular for patent applications on an international level, licensing agreements) as well as market entrance and marketing of the products or services of the biotech company on an international level.

There are a few additional venture capital companies active on the Estonian market (e. g. LHV Ventures), but they did not invest in biotech companies so far but concentrate their investments on manufacturing firms or the IT sector. The high risk of biotech companies, relatively high investment sums in the biotech field, the needed mid-term investment perspective, lack of business orientation in a lot of Estonian biotech companies, the necessary high extent of company assistance as well as lack of knowledge and missing experience with the biotechnology and pharmaceutical field were mentioned by the interviewees as main reasons for not dealing with biotech investments. In addition, the low number of biotech companies in Estonia was highlighted during the interviews which does not allow a venture capital investor to sufficiently diversify the investment portfolio in the life sciences field. Lack of exit opportunities for venture capital companies was regarded as another constraint since an IPO of a biotech company at the Tallinn Stock Exchange does not seem to be realistic in the coming years and pharmaceutical companies which might be interested to buy an Estonian biotech company do not exist in this country.

In Estonia, hardly any venture capital is available for the pre-seed and seed phase of companies in particular in high technology fields. Again the high levels of risk of companies which have been just founded was mentioned as the main reason for the low amount of available investment capital for these early stages. In particular in the biotechnology field seed-financing was regarded as a high-risk business which needs a "long financial breath" and specific experience in the biotechnology and pharmaceutical field which does not seem to be available in the venture capital companies active in Estonia.

Most of the venture capital companies active in Estonia concentrate their own fund-raising activities on private investors sometimes in the Baltic States but also in other European countries or the USA. The lack of institutional investors in Estonia as well as the other Baltic States was mentioned as the main reason by the interviewees for concentrating on private money. Some Estonian and international private investors are active in financing biotech companies in Estonia as well – either directly or via specific investment banks. But most of these investors do not have specific experience in biotechnology. In addition, it was highlighted during the interviews that private investors in Estonia are extremely short-term oriented what hinders direct investments in biotech companies but also complicates fund-raising activities of venture capital companies within Estonia. Partly private investors seem to have unrealistic expectations on returns of investment in biotech companies as well.

The Tallinn Stock Exchange was founded in 1996 reaching a transfer volume of 14.1 billion EEK in 2000 (Bank of Estonia 2000). With only 19 medium and large companies listed on the Tallinn Stock Exchange, financing via an IPO is not regarded as a realistic option even for mature biotech companies in the coming years in Estonia. This implies that an IPO at Tallinn Stock Exchange does not seem to be a realistic exit possibility for a potential VC investor in an Estonian biotech company. Interviewees stressed the lack of institutional investors as well as the low trade volume at the Tallinn Stock Exchange as the most important hindrances in this respect.

Another financing possibility represents the acquisition of all or part of the equity of a biotech company by another biotech company or a company of potential application industries, often the pharmaceutical industry. Due to lack of "mature" biotech companies and the missing of an R&D-oriented pharmaceutical industry in

Estonia (see chapter 2.4.1), mainly international companies would have the financial resources to buy in into Estonian biotech companies. However, current strategies of international pharmaceutical and biotech companies tend to acquisition of such biotech companies which have a strong product pipeline (in particular in clinical development and phase II or III-trials) or companies which generate already significant turnover with approved (pharmaceutical) products. Both prerequisites are currently not fulfilled by Estonian biotech companies and it should not be expected that they will develop to such a status in the coming years. With regard to potential co-operation agreements between Estonian biotech companies and international biotech or pharmaceutical companies, one should have in mind that currently most of the international players tend to arrange their co-operation agreements very flexibly without taking an equity stake in the co-operating biotech companies.

In general, access to financing can be regarded as a considerable constraint for SMEs in Estonia. In a survey among manufacturing SMEs in 1998 financing issues were one of the most important problems of the participating firms. In particular they highlighted high-loan interest rates, the limited availability of investment loans, the low availability of collateral that was acceptable for financial institutions and a shortage of loans for working capital (Phare 1999). Although the range of instruments for company financing offered by private banks seem to widen in recent years (e. g. by the introduction of leasing possibilities), insufficient collateral remains a problem for SMEs, constraining their ability to access bank loans in many cases since private banks ask for collaterals which significantly exceed the value of the loans in order to keep the exposure to risk of the bank to a minimum. This means that private banks in Estonia tend to invest only in low risk companies, so that bank loans to start-up companies or technology-based firms are the rare exception because of the higher risk involved (Anonymous 2002). This view was completely shared by the interviewed biotech companies and scientists being active as company founders who reported that it is almost impossible to get a commercial bank loan for a biotech company in Estonia. A specific constraint represents the collaterals requested from the banks which can hardly be provided by biotech companies which mainly invest in R&D activities and not e. g. in manufacturing equipment. In addition, biotechnology has a high-risk image in banks and the time perspectives of many biotech projects are too long in comparison to the rather short-term loans which are often offered from commercial banks.

Altogether, it can be stated that low availability of private financing possibilities and a limited set of (commercial) instruments in this area represent a major constraint for company founding and growth in the biotech field in Estonia. This aspect gains importance if the specific difficulties of start-up biotech companies are considered to provide collaterals for commercial bank loans (preventing in fact the use of this instrument in most cases), as well as the long financing time periods and the substantial investment sums required in particular in the biomedical field (e. g.

for drug development). Another specific constraint represents the extreme short-term view of potential Estonian private investors which does not match with the needs of most biotech companies for mid- or long-term financing.

2.3.2 Public financing of business activities

After the re-organisation of the recent Estonian Innovation Fund, whose organisation and procedure were criticised as being complicated and not efficient (Hernesniemi 2000) the Estonian Technology Agency (ESTAG) was established in 2001 in order to develop Estonian business through the support of technological and innovative projects (ESTAG 2002a). ESTAG is one of seven agencies that form Enterprise Estonia and administers the financial means which are allocated to innovation policy by the Ministry of Economic Affairs and Communications of Estonia.

The aim of ESTAG is to support the development of innovative products and services in Estonian companies as well as to assist research institutions in conducting technology and innovation-oriented applied research projects. For this purpose ESTAG offers three different ways of financing:

- Grants for conducting feasibility studies
- Grants or loans for conducting applied research
- Grants or loans for conducting product development

A feasibility study has the purpose to prepare applied research or development projects and obtain information about the practicability of a planned project. Another possibility is the funding of a high-risk part of a larger applied research project within a feasibility study. Both research institutions and companies can apply for a feasibility study up to maximum costs of 100,000 EEK. Feasibility studies are always financed with a grant which can reach up to 75 % of the expenses of the feasibility study. According to the estimations of interviewees biotech companies generally have no specific difficulties to arrange the requested own financial contribution for feasibility studies, while research institutions face higher difficulties in this respect since they have lower free cash reserves, and therefore try to use personnel who is financed form other sources for this purpose.

Applied research projects aim at developing new or to substantially improve already existing products, technologies or services. In general, such projects have a duration of two to four years and can be applied for by research institutions and companies. For research institutions ESTAG finances applied research projects with a research grant up to 100 % of the costs directly related to the project. For companies financing is provided either in form of a grant (up to 50 % of the project expenses, in case of SMEs up to 60 %) or a loan which can cover up to 75 % of the direct costs of the project. The interest rate for the loan ranges between 1 % and 5 % (in average around 3 % according to interviewees' information) compared to a commercial interest rate of around 8 %. According to interviewees there are no clear and valid rules and principles for the level of the interest rate which a single company has to pay for an ESTAG loan. The maturity term of the loan can last up to eight years with a grace period for the loan principal of maximum three years. Another advantage represents the fact, that no collateral is required for an ESTAG loan.

Product development projects aim at the conviction of the results of applied research projects in the new products, technologies or services or the substantial alteration of existing ones. In general, such projects can last up to an industrial prototype. Only companies can apply for product development projects which are generally financed using ESTAG loans which can cover up to 75 % of the total project expenses. Grants which are rarely used in product development projects can cover up to 25 % of the total direct costs of the project (with an extension possibility of 10 % for SMEs).

Before applying for a project ESTAG strongly advises potential applicants to consult the specialists of the institution in order to improve the quality of the project proposal as well as to ensure the compatibility with the financing conditions of ESTAG. In general, this consultation possibility was appreciated by the interviewees of biotech companies and research institutions but some criticised the low knowledge and lack of experience with the specific needs of biotechnology-related projects at ESTAG.

Project proposals can be submitted to ESTAG all over the year without fixed deadlines. Application for projects are submitted with the help of a specific formula which includes a project description and in case of companies information related to the company strategy. The project plan includes information to the scientific and technical background of the project, the foreseen working steps, project partners, cost calculation and budget, potential risks of a project as well as a realisation strategy. Companies have to provide additional information related to their financial situation and development, profit and loss calculations as well as the business strategy. In addition to some formal attachments to the project description, companies are asked to deliver their business plan to ESTAG which should contain information related to e. g. markets, competitors, market entrance strategies, expected turnover and cash-flows.

The evaluation of project proposals is done by ESTAG specialists (in terms of cost and economic aspects) in co-operation with mostly Estonian external scientific and technical experts. The evaluation is based on the information provided in the application documents, partly additional meetings with the applicants are organised to clarify open questions or get more detailed information. Based on the results of the internal and external evaluation the ESTAG specialist elaborates an internal report to the different ESTAG committees which finally decide on project funding. This report contains information about the used technology/scientific approach, the developed products or services, human resources and expertise of the applicant, marketing issues, cost calculation and budget as well as the impacts of the project on the Estonian economy and society. In addition, a suggestion of project funding is submitted within this report.

Based on the financial volume of the project application, ESTAG has different committees responsible for decision about project funding. Up to a project volume of 350,000 EEK the so-called "project group" (consisting of the general directors of ESTAG, Estonian Investment Agency and the Regional Development Agency) is taking this decision, while projects ranging from 350,000 EEK up to 10 million EEK are handled by the "Financial Committee" which includes additionally representatives of different ministries. In most cases the responsible committee seems to follow the suggestions concerning project funding provided by the internal ESTAG specialist, but sometimes substantial changes (e. g. relationship between loans and grants, level of the interest rate, setting some conditions in the contract) are realised by the responsible committee. The financing of the accepted projects by ESTAG is based on reaching defined interim results within the course of the project.

The total volume of the portfolio of R&D projects of ESTAG amounted to 375.8 million EEK at the end of 2001, of which co-financing of ESTAG comprised 114.1 million EEK. Among the ESTAG financing loans comprised to 61.8 million EEK and grants to 52.3 million EEK (ESTAG 2002a). Bio- and food technology has a high relevance in the project funding of ESTAG since around 36 % of all financing decisions which have been taken during 2001 related to this field. This amounted to a total sum of 17 million EEK for three projects (ESTAG 2002a). Funded institutions of ESTAG in the biotechnology field include the biotech companies Asper Biotech, Biodata OÜ and Quattromed as well as the Institute of Microbiology and the Institute of Molecular and Cell Biology of Tartu University in the research area (ESTAG 2002b).

The interviewees regarded the application procedure for ESTAG funding as demanding but most of the interviewed experts agreed that it can be realised with reasonable efforts using the support provided by ESTAG. Several interviewees criticised the evaluation procedure of ESTAG. In particular it was argued that the scientific and commercial "scene" in biotechnology is rather limited in Estonia so that independency of the evaluating scientific and technical experts as well as confidentiality of the information provided cannot be guaranteed in all cases. In addition, it was seen as problematic if the ESTAG consultant of a specific project application has a high influence on the decision whether to fund the project or not. Furthermore, it was argued that this means in practice that an economic specialist has a high influence on project funding in the life sciences field without having the necessary scientific background.

According to interviewees' information there seems to be a rather high acceptance rate of project applications at ESTAG. Some interviewees estimated this rate up to 70 % and expressed the view that there seems to be more money available at ESTAG in some fields than application for high-quality projects. In contrast, interviewees criticised that ESTAG only supports product development projects but cannot offer (co)financing of patent applications at non-Estonian patent offices, market introduction of products or services or marketing activities e. g. outside Estonia. Another problem represents the fact that the procedures at ESTAG seem to take much longer than three months which are foreseen in ESTAG's regulation. Many interviewees reported about time periods of six months and more from submission of a proposal at ESTAG to the final funding decision.

SPINNO programme

The SPINNO programme which is operated by ESTAG is one of the connecting activities of the Ministry of Economic Affairs and Communications for further liaisons between scientific institution and companies. The programme started in 2001 and will be completed by the end of 2003. For this time period a budget of 29 million EEK is available. The objective of the SPINNO programme is to promote the implementation of scientific results in business activities. In this sense the programme supports activities of Estonian universities and research institutions in the following areas:

- Increase the extent of research results of Estonian universities and research institutions which are applied in commercial companies
- Develop an environment which fosters entrepreneurship and entrepreneurial spirit in Estonian universities and research institutions
- Develop co-operations between Estonian universities and research institutions and technology- and science-oriented companies

The different universities and research institutions in Estonia have differently reacted on the SPINNO programme. Tallinn Technical University started its SPINNO activities in 2001. Research projects between university institutes and industry are administratively supported within this programme. In addition, the university defined rules concerning the handling of IPR issues between the individual researcher and the university and gives administrative assistance for patent applications at the Estonian Patent Office. For this purpose an IPR specialist has been hired at the R&D department of Tallinn Technical University who consults external patent attorneys if required. Generally, the university prepares the documents necessary for patent application in co-operation with the inventor. In case foreign patent applications are concerned, these will be handled with the help of a patent attorney located in the respective country. Financing of such a specialist was regarded as the major problem. Furthermore, legal and administrative advice and support is given for company founders by this department. In order to raise awareness and knowledge of potential company founders, specific workshops and training activities have been organised by Tallinn Technical University. Interviewees highly appreciated the support given by the R&D department of Tallinn Technical University in order to facilitate common research projects industry as well as to support patent application of scientists. However, only very few interviewees at Tallinn Technical University had experiences with the SPINNO project so far.

The SPINNO programme initiatives of Tartu-based organisations elucidate limited co-ordination of activities in this region. According to information given by the interviewees there have been SPINNO proposals from the Tartu Science Park, Tartu University as well as the Agricultural University in Tartu which partly suggested the same activities (e. g. to hire and educate an IPR specialist at the single institution). Due to this lack of co-ordination and joint activities, no SPINNO project is funded in Tartu so far.

Therefore, the Estonian Biocentre in Tartu initiated a specific BIOSPINNO activity which includes several institutes of Tartu University, the Agricultural University in Tartu, Tallinn Technical University as well as Tallinn-based KBFI. In addition, some biotech start-up companies are incorporated in this initiative as well. According to interviewees activities of the BIOSPINNO initiative aim at improving IPR advice in the life sciences field, supporting co-operations of research institutions and companies on a national and international level as well as supporting of fund acquisition from international sources. Interviewees assessed it as being positive that all key actors in the biotechnology field are involved in this activity in spite of the "competition" between Tartu and Tallinn-based institutions in this field. At the time of the interviews the proposal of BIOSPINNO was submitted to ESTAG but no decision was taken so far.

Competence Centre Programme

In addition to the SPINNO programme the Ministry of Economic Affairs and Communications launched the Competence Centre Programme in 2002: this programme was agreed from the Estonian Parliament in autumn 2002 so that its implementation can start at the end of 2002. The programme aims at bringing together the science and industry sectors, integrating the environments with different traditions and frames of acting and developing their co-operation (Ministry of Economic Affairs and Communications 2002). For this purpose it is foreseen to establish several competence centres[9] as a strategic co-operation between science and industry partners based on their R&D competence and conducted in a specific technological field. The centres must have a clear research focus in the defined field and should include a core group of an employed director, around three full-time researchers or engineers and additional PhD or master students (Ministry of Economic Affairs and Communications 2002). In the mid-term industrial companies shall take the leadership in the established centres and contribute with employed R&D personnel. Due to lack of companies with established R&D departments in Estonia (Kurik et al. 2002) companies can participate in the beginning in a competence centre by providing financial support.

A two stage application procedure is intended for the programme. In a first phase short proposals can be submitted which will be internally evaluated by ESTAG experts. It is intended to financially support submission of a final project application of all "reasonable" short proposals up to 300,000 EEK. For providing final project applications a timeframe of around three months is foreseen, so that interviewees estimated that the first competence centres might start their work at the end of 2003. Several interviewed experts of research institutions active in the biotechnology field intended either to co-ordinate a consortium to establish a competence centre or to participate in such an activity. However, the success of such initiatives cannot be assessed at present so that the impacts of this programme on the commercial exploitation of research results in the biotech area cannot be estimated either.

Support to conducting international projects and partner finding activities

In addition to its activities targeted only to Estonia, ESTAG supports preparation of internationally oriented R&D projects as well. In this context the agency assists interested companies or research institutions in finding appropriate co-operation partners in foreign countries. One instrument is the Estonian Innovation Relay Centre programme (ESTRIC) which aims – as part of the European Innovation Relay Centres – at increasing competitiveness of Estonian companies and research institutions and promoting their participation in international programmes. Within Estonia ESTRIC is co-ordinated by the Tartu Science Park Foundation. Besides ESTAG the Archimedes Foundation and the Tallinn Technical University Innovation Centre Foundation are partners in this programme. The most important activities of this network relate to technology auditing, international partner search (using a technology-based database within the European IRC network), information and advice about specific EU programmes, assistance of companies or research institutions during contract negotiations as well as organisation of technology-oriented co-operation events.

---

9 Interviewees estimated that between four and five competence centres might be established given the available budget of 25 million EEK and the requirements which have to be fulfilled by the centres.

In addition, ESTAG is responsible for running the EUREKA programme in Estonia. Estonian partners of international projects which are financed within the EUREKA programme of the EU are supported by ESTAG's grants or loans. In addition, ESTAG tries to find co-financing for internationally oriented projects. An additional contact point for the EUREKA programme is established at the Archimedes Foundation which recently represented the entire 5th Framework Programme of the EU.

The Archimedes Foundation was founded by the Ministry of Education in 1997 to implement EU PHARE and Socrates programmes. Currently the Foundation has 24 employees and is hosting different programmes concentrating on supporting information society developments (Archimedes Foundation 2002). Within the 5th Framework Programme of the EU Archimedes Foundation was national contact point of this programme in Estonia as well as Innovation Relay Centre of the EU.

The Estonian Investment Agency (EIA) as part of Enterprise Estonia is concerned with creating a positive image of Estonia as a potential location for investment in foreign countries. This includes marketing the location Estonia in target sectors and target countries, providing services for potential investors and providing aftercare services for foreign investors already operating in Estonia. So far biotechnology does not play any substantial role in the marketing activities of EIA but it is intended to increase efforts in this area in the coming years. However, EIA was not known by the interviewees active in the biotechnology field in Estonia, although they asked for enhanced joint biotechnology-related marketing activities in foreign countries in the coming years.

2.3.3 General framework of business activities

The environment for company foundation and enterprise development was regarded as being rather favourable in Estonia according to the views of the interviewees and several research projects carried out in recent years. The procedure of company registration is regarded as being efficient (DG Enterprise of the European Commission 2001) and did not cause specific difficulties to the interviewed biotech companies. Interviewees stated as an additional advantage that rather low equity sums have to be brought in as guarantee in companies (e. g. 40,000 EEK for a limited company) which can be invested in form of real estate or equipment as well.

According to the interviewees' estimations the relatively simple and transparent taxation system forms another part of the rather favourable business environment in Estonia. In this context the corporate income tax of 26 % was highlighted. From the year 2000 it has been reduced to 0 % for all profits and revenues re-invested in the business – this was highly appreciated by the interviewees and seen as a measure to promote investments and develop business activities in all economic fields. Some interviewees stated that in practice most companies do not pay substantial corporate income taxes due to the existing tax rules. The 18 % VAT rate in Estonia is comparable to other candidate countries (Estonian Institute for Futures Studies 2001) with a rather broad tax base. Exports are promoted by a 0 % VAT rate on exports. In addition, SMEs have the possibility to exclude themselves from registration for VAT if their monthly turnover is below 230,000 EEK. This is true for at least part of the biotech companies in Estonia.

In contrast to the corporate tax system, single interviewees expressed a rather critical view in relation to the social security system in Estonia. The social security tax has been established to provide social security to employed persons. Currently only the employer is in charge to pay social security tax, but there are discussions that the liability for social security guarantees will be divided between employees and employers in future. The social security tax is generally 33 %, from which 20 % is submitted to social insurance and 13 % to the national health insurance. In addition, a 0.5 % insurance rate for unemployment and a 1 % rate for professional association insurance have been introduced in 2002. In particular the latter two amendments of the social security system have been criticised by some interviewees as being only another activity of public authorities to increase tax burden of citizens and employers without any real return favour.

2.4 Demand/social acceptability network

The situation and important developments relevant for the demand side of modern biotechnology within and outside Estonia are analysed within this network. Therefore, at the beginning information are summarised related to the markets of Estonian biotech companies and their market orientation (for details see chapter 2.2.4). Afterwards the situation and innovativeness of potential applications industries of modern biotechnology is analysed followed by the legal framework and public acceptance issues of modern biotechnology in Estonia.

As outlined in chapter 2.2.4 Estonian biotech companies are primarily export oriented and focus to a high extent on the (bio)medical and healthcare market. Within Estonia the market for biotech companies is hardly existing mainly due to the missing of a strong domestic pharmaceutical industry, while most biotech firms are focusing on diagnostics and therapeutics. Some Estonian biotech companies, like e. g. Quattromed, generate some turnover with services for hospitals and surgeries or sell some materials to Estonian research institutes. Most of these business activities are based on personal contacts and networks which is facilitated due to the small size of Estonia and the limited number of persons active in the relevant fields. For the coming years increasing market opportunities for Estonian biotech companies are expected also within Estonia if the Estonian Genome Project will lead to a success.

The international markets of Estonian biotech companies are extremely heterogeneous and scattered. At present some European countries and the USA are the most relevant countries as target markets for Estonian biotech firms. The slowdown of the biotech industry in these countries in the last two years has impacts on Estonian biotech companies, too, since some companies reported loss of clients or in some cases total markets. Most of the business contacts of Estonian biotech companies also on an international level are based on personal networks and contacts in particular in the scientific arena. Single biotech companies also try to operate on international markets via external distributors. So far only one Estonian biotech company reported about foreign subsidiaries in order to cover their most important international markets.

One of the most important weaknesses of most of the Estonian biotech firms is their lack of strategic planning and missing marketing strategies. In addition, firms rely on very few customers, which is bound to create problems in case a major customer is lost – which happened already to several of the interviewed firms. Often company founders or "managers" do not have the skills or experience to systematically analyse the situation and development of potential markets, the needs of their (potential) customers and the activities of their competitors, develop strategies how to approach new customers or to enter international markets, to know and/or use common marketing instruments and to adopt those to changing environments. Another problem is the missing "business orientation" in at least half of the Estonian biotech companies which is characterised by a risk-averse attitude of the company owners, a missing growth strategy and often only part-time engagement of the key personnel of the company. In both areas there is strong need for improvement of the skills of the company founders and the managers of Estonian biotech companies, in order to use the existing market opportunities within and outside Estonia to a higher extent and to decrease the risk of company collapses, which are not unlikely if the substantial management skills are lacking in the key personnel of a company.

2.4.1 Potential application industries of modern biotechnology

Modern biotechnological methods, tools and products can be used in a variety of traditional industries. The most important one are the pharmaceutical and chemical industry, agriculture and food processing, environmental technologies, biomedical equipment and supplies as well as wood processing and pulping. Analyses of macro-economic and employment effects of modern biotechnology in other European countries indicate that these traditional industries are important carriers of the overall economic potential of modern biotechnology and that e. g. much higher employment effects are observed in these industries compared to specialised biotech enterprises (Wörner and Reiss 2001, BMBF 2000). Therefore, the situation of these industries in Estonia is analysed in the following taking into account their interest in innovations in general and in modern biotechnology in particular.

Pharmaceutical industry

Globally, the pharmaceutical industry is the most important application area of modern biotechnology. In particular gene sequencing and genomics activities are regarded as new key elements in drug discovery and development. In addition, biopharmaceuticals represent a growing segment in the most important pharmaceutical markets. Almost one third of the approved pharmaceuticals in the EU belong to this group (Hinze et al. 2001), while the corresponding figure reached almost 25 % in the USA in 2000 (PHRMA 2001). Experts estimate that all new pharmaceuticals will come in touch with modern biotechnological methods or tools in the coming years. This highlights on the one hand the important role of this technology for drug discovery and development, on the other hand it underlines the high relevance of the pharmaceutical industry for commercial exploitation of scientific findings in this area.

According to the interviewees no R&D-oriented pharmaceutical industry exists in Estonia. There are a few generic and plant pharmaceutical-producing companies as well as sales subsidiaries of multinational pharmaceutical companies in Estonia. A recently finalised study estimated a total of 11 producers of drugs and biomaterials in Estonia (Scandinavian Care Consultants 2002). The most important domestic pharmaceutical company is Tallinn Pharmaceutical Company which is the oldest manufacturer of medicinal products in Estonia (founded in 1914). Currently the Company has around 200 employees. Tallinn Pharmaceutical Company is the only producer of medicines and drugs in Estonia operating with a full production cycle and manufactures more than 50 different product items like medicines, semi-medicinal products, natural products and food additives. In 2000 the Company had an annual turnover of 102 million EEK with domestic sales of around 24 million EEK. The most important market for the Company is Russia with a turnover share of around 67 % in 2000 (Tallinn Pharmaceutical Company 2002). The Company is mainly a producer of generic drugs without an own drug discovery programme. R&D activities are mainly focused on improvement of the production process as well as clinical trials which are necessary to show efficacy of the generic form of an original pharmaceutical.

Since 1999 the Latvian pharmaceutical company Grindex holds a majority share of the stocks of Tallinn Pharmaceutical Company. During the interviews the impression arose that Grindex is controlling the activities of Tallinn Pharmaceutical Company to a high extent and that the Estonian company lost most of their "entrepreneurial independency". In this direction tends also the 2001 signed concern agreement between Grindex and Tallinn Pharmaceutical Company. According to this agreement Grindex "will develop the mutual strategy of concern activities" and "keep the exclusive rights to sell the products of Tallinn Pharmaceutical Company in all the export markets" (Grindex 2001).

The Swedish pharmaceutical company Nycomed invested around 2 million EEK in Nycomed Sefa (Estonian Investment Agency 2001b), which is located in Põlva and employs between 50 and 100 people (Scandinavian Care Consultants 2002). According to information provided by the interviewees, all the other very few companies of the Estonian pharmaceutical industry are rather small sized and do not carry out substantial R&D activities. Altogether, it has to be stated that modern biotechnology does not play a role in the few pharmaceutical companies in Estonia so far.

Chemical industry

The chemical industry has been one of the most important industrial sectors in Estonia for years. The output of the chemical industry amounted to around 3.08 billion EEK in 2000 and equalled to 6.6 % of the total production of the manufacturing industry. Based on local Estonian raw material (Estonian Oil Shale) the Estonian chemical industry mainly concentrates on production of shale oil, ammonia, mineral fertilisers and oil-based bulk chemicals. In the latter field in particular the Viru Keemia Grupp Ltd. (Viru Chemical Group) is active, while Nitrofert Ltd. represents the main producer of ammonia and mineral fertilisers (Estonian Investment Agency 2001b). Another interesting company represents AS Silmet Group as a producer of rare metals with an estimated turnover of more than 650 million EEK in 2001 (AS Silmet Group 2002). Additional fields of activities of the Estonian chemical industry which might be of relevance for use of modern biotechnology are the production of paints and varnishes as well as detergents. Mainly small and medium-sized enterprises are active in these fields which are more consumer oriented than the producers of bulk chemicals or minerals. According to the interviewees agro-chemical products which might be interesting for application of modern biotechnology are not developed and produced in Estonia.

The chemical industry of Estonia is very export oriented since almost three quarters of the production of chemicals and chemical products in 2000 were exported mainly to Latvia and Lithuania, the EU and some CIS countries. However, analyses of the export structure of the Estonian industrial production of 2000 compared to the time period of 1995 to 1996 indicate that the capital- and technology-intensive parts of the chemical industry (like production of chemicals or rubber and plastics) are relatively uncompetitive among the Estonian industrial branches, while Estonia revealed competitive advantages in the resource-intensive production of fuels (Tiits et al. 2002). Like the other potential application industries of modern biotechnology the chemical industry has experienced a strong restructuring process with a significant decrease of the labour force from around 7,000 people in 1997 to around 4,600 at the beginning of 2000 (Estonian Investment Agency 2001b). This strong decrease in the number of employees resulted in a labour productivity which is more than twice higher in the chemical industry compared to the manufacturing industry of Estonia as a whole.

The Estonian chemical industry attracted foreign direct investments slightly below average of the total manufacturing industry of this country (Sinani and Meyer 2002). Examples of foreign companies which have invested in Estonia are Dynamit Nobel, Kemira, Benckiser and Procter & Gamble (Estonian Investment Agency 2001b). Companies owned by foreign investors outperformed domestic firms of the chemical industry in particular in the capital intensity and labour productivity, while export rates are almost equal between these two groups (Sinani and Meyer 2002).

According to the data of the CIS survey from 1998 to 2000 between 30 % to 49 % of the manufacturers of oil shale products and rubber and plastic products were regarded as being innovative. Their innovativeness was below those of the manufacturers of chemicals in which more than half of all enterprises were identified as innovators (Kurik et al. 2002). This view was shared by several participants of the face-to-face interviews who regarded mainly some small and medium-sized enterprises in the (fine) chemical area as innovative, while in particular the manufacturers of oil shale products and oil-based bulk chemicals were classified as "typical cost cutters" by the interviewees. With the exception of a specific co-operation between Tartu University, Tallinn Technical University and AS Silmet Group (DG Enterprise of the European Commission 2001) and some smaller co-operations between scientists active in the chemistry area and some smaller chemical companies, most interviewees expressed the view that there are very limited innovation activities in the chemical industry in Estonia so far. This relates as well to the use of modern biotechnological methods, tools and products.

Biomedical equipment

According to a recently finalised study there are 42 manufacturers of medical devices and 115 companies selling medical devices located in Estonia (Scandinavian Care Consultants 2002). Among those is Tondi Elektroonika AS which produces electro-accoustical hearing aids with more than 100 employees in Tallinn. The relevance of biomedical equipment and supplies cannot be figured out from the results of this study. According to the interviewees there are only very few small and medium-sized manufacturers of biomedical equipment and supplies which often are concentrated on specific techniques or market segments. In general, they do not carry out wide-ranging R&D activities in particular not related to modern biotechnology.

Agriculture and plant breeding

Estonian agricultural policy changed sharply at the beginning of the 1990s: from highly subsidised agricultural production to virtually unsubsidised production with a free price formation. As a result, employment in the sector decreased, as did the relative share of the added value of agricultural products in the gross domestic product (GDP). In 2000 the added value produced in agriculture and hunting amounted to 2,784 million EEK which equals to 3.6 % of the Estonian GDP (table 2.15). According to the Statistical Office of Estonia 31,500 people were employed in agriculture and hunting in 2000 compared to 114,600 people in these sectors in 1992 (Ministry of Agriculture 2002). The 2000 number equals to 5.2 % of the total employment in Estonia (table 2.15).

Table 2.15: Relevance of agriculture in Estonia

	1996	**1997**	**1998**	**1999**	**2000**
Added value of agriculture (mio EEK)	2,722.6	2,779.5	2,810.0	2,584.2	2,784.1
Relative share in GDP	5.8 %	4.9 %	4.3 %	3.7 %	3.6 %
Employment in agriculture (1,000)	52.1	44.8	43.5	38.2	31.5
Employment of total	8.1 %	6.9 %	6.9 %	6.2 %	5.2 %

Source: Ministry of Agriculture 2002

In plant production, the area under field crops was 745,000 ha in the year 2001. The majority of this was cultivated with grains (270,000 ha), rape and turnip rape (27,500 ha), potatoes (22,000 ha), leguminous vegetables (3,500 ha) and open field vegetables (3,300 ha). Perennial grass plants were grown on 390,000 ha. In addition, there were 341,000 ha of unused arable land and 33,600 ha of lay fallow (Ministry of Agriculture 2002). Another important field are the production of fruit and berries for which part of the needed plants are produced with the help of biotechnological methods. In livestock production the number of cows decrease significantly since the beginning of the 1990s to around 129,000 cows in 2001. More than 90 % of the dairy farmers had less than 10 cows in 2001, while in contrast the 240 agricultural holdings with more than 100 cows kept around 56 % of all dairy cows in Estonia (Ministry of Agriculture 2002). In addition to milk and beef production, pigmeat and sheepmeat production as well as poultry farming represent other relevant fields in livestock production in Estonia.

According to information provided by the interviewees Estonian farmers use certified seeds and hybrid varieties only to a low extent mainly due to cost reasons. Due to lack of know-how and technical shortcomings, hybrid varieties are not developed in Estonia so far, so that the respective seeds are imported. In addition, there are only very few private plant breeding companies in Estonia due to the small size of the Estonian seed market. A public research institute under the head of the Ministry of Agriculture has developed some plant varieties which are registered for the Estonian market. In addition, several EU plant-breeding companies (mainly from Germany, Finland or Sweden) are active on the Estonian seed market as well. Due to the long and hard winter in Estonia, almost no winter varieties of agricultural crops are used e. g. in cereals or rape in this country. Modern biotechnology but no genetic engineering tools have a certain relevance in the breeding and reproduction of plants (e. g. potatoes, specific berries) in Estonia. But no field trial with genetically modified plants has been carried out in Estonia so far. In addition, there is no approval for commercialisation as well as no commercial growing of such plants.

Food-processing industry

Since the independency of Estonia, the food-processing industry has been transformed from large-scale production units whose food production was mainly targeted to the Soviet Union market to a widely diversified industry branch with a high number of SMEs. The food-processing industry has traditionally been the largest industrial sector in Estonia. Since 1994 the output of the food industry increased by around 50 % to 9.7 billion EEK (table 2.16) which is equivalent to 24 % of the gross industrial output of Estonia (Ministry of Agriculture 2002). During the industrial restructuring since 1992 the share of the production of food and beverages in total industrial production has substantially decreased (Tiits et al. 2002). In parallel, the number of employees in the food industry has continually decreased from nearly 24,000 people in 1994 to around 14,800 in 2001 (around 18 % of the employees in the total processing industry) (table 2.16). During this time period the share of the food industry in industrial output of Estonia decreased as well from more than one third at the beginning of the 1990s to around one quarter in 2000 and 2001 (figure 2.15). In the recent three years between 27 % and 28 % of the Estonian food-processing industry's products have been exported (table 2.16) which is significantly higher than the export rate of the food industry in most EU member countries.

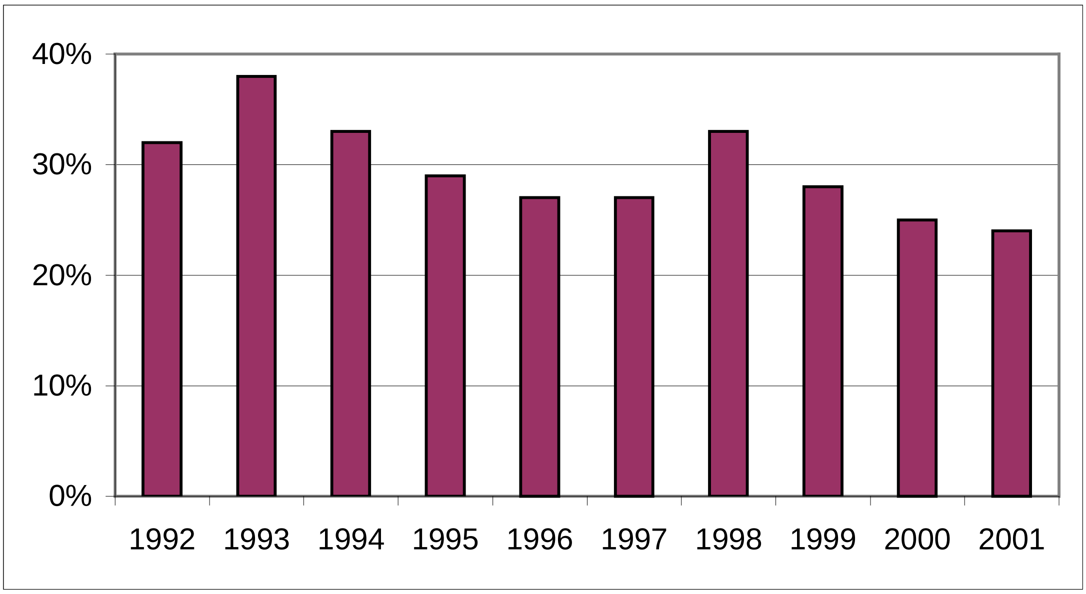
Table 2.16: Food industry's gross output, employment and share in export

	1994	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**
Gross output of food industry (EK '000,000)	6,513	7,554	8,534	10,903	10,802	8,433	8,727	9,736
Meat and meat products	1,382	1,221	1,241	1,237	1,454	1,533	1,380	1,605
Fish and fishery products	627	1,156	1,039	1,492	2,055	1,938	1,349	1,386
Dairy products	1,195	1,368	1,883	2,260	2,983	3,022	2,435	2,851
Flour and cereals	51	62	79	91	87	103	58	76
Ready-made fodder	363	361	292	246	351	412	299	263

Bakery products	507	606	756	929	984	995	759	898
Beverages	890	1,091	1,546	1,566	1,806	1,721	1,874	1,709
Employment in food industry (% of the employed in processing industry)	23.8	24.6	23.7	24.4	24.5	21.5	19.9	17.9
Export of food industry in millions of EEK	2,028	1,496	1,977	3,543	3,735	2,417	2,392	2,742
Share in total export %	12.3	7.1	7.9	8.7	8.2	5.6	4.4	4.7

Source: Statistical Office of Estonia (cited in: Ministry of Agriculture 2002)

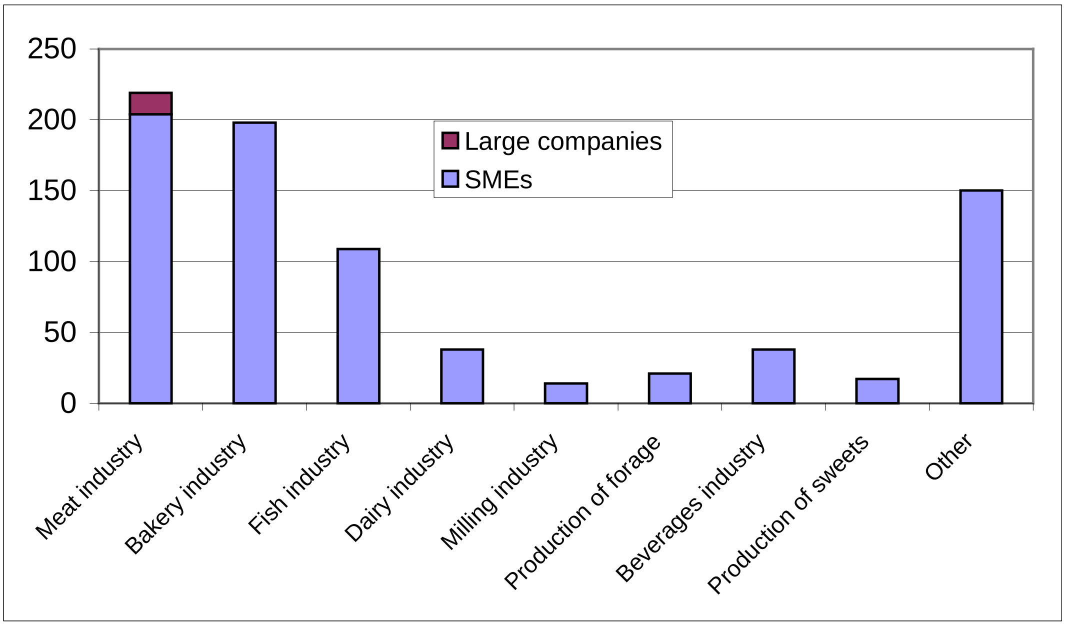
Figure 2.15: Share of food industry in industrial output in %



Source: Ministry of Agriculture 2002

In 2001 the dairy industry accounted for 29 % of the output volume of the Estonian food industry (Ministry of Agriculture 2002) with 38 companies being active in this field (figure 2.16). In terms of output volume, the production of beverages is the second-largest branch of the food industry in Estonia with a share of 18 % in 2001 (Ministry of Agriculture 2002) and 38 active companies (figure 2.16). Other important branches of the Estonian food industry are the meat industry (with 16 % of the production volume and almost 220 production facilities) and the fish industry (with 14 % of the production volume and more than 100 companies) (Ministry of Agriculture 2002, figure 2.16). In terms of employees, the fish-processing industry was responsible for more than one quarter of all employees in the food-processing industry in 2000 followed by the dairy industry with a share of almost 20 % (Estonian Investment Agency 2001a). In addition, the bakery industry turns out to be rather personnel intensive with around 17 % of the employees and only 9 % of the total turnover of the food industry in 2000 (Estonian Investment Agency 2001a). While the meat industry and the beverages industry showed a labour productivity above average in 2001, resulting in monthly salaries of the employees which in particular in the production of beverages exceeded the average salaries in the food industry by more than 50 % (Estonian Investment Agency 2001a).

Figure 2.16: Number of enterprises in food industry in 2001



Source: Veterinary and Food Board (cited in Ministry of Agriculture 2002)

Between 1999 and 2001 nearly 1.2 billion EEK were invested in the Estonian food industry, the majority of the investments was spent on the construction and re-construction of enterprise buildings and premises (Ministry of Agriculture 2002). It was estimated that approximately the same sum or even higher investments are necessary to bring all food industry enterprises into conformity with the requirements of the new Food Act (which will be put into force at the beginning of the year 2003) and forthcoming EU regulations. A lot of investments have been done in recent years, in addition, in purchasing new machinery and equipment in order to raise productivity of Estonian food industry companies (Kurik et al. 2002).

Part of these investments came from foreign capital as well. Foreign investments in the food industry in Estonia have been concentrated on the brewing industry were the net turnover of foreign invested enterprises accounted for almost 80 % of the net turnover of the sector (Ministry of Agriculture 2002). Other important targets of foreign investments have been meat industry, dairy industry and bakeries, while

e. g. the fish industry has not attracted foreign investors todate (Ministry of Agriculture 2002). According to information given during the interviews the main reasons to invest in the food-processing industry in Estonia are low production costs, a liberal trade policy, low taxes (in particular a zero tax on invested profits), local raw material basis, increasing market opportunities as well as the geographical location between Scandinavia, Russia and the EU. Foreign owned firms in the food industry outperform domestic firms e. g. in terms of capital intensity, labour, productivity and export rates (Sinani and Meyer 2002). Estonian interviewees expressed the opinion that a foreign ownership can result in advantages as well as disadvantages for the Estonian company. In particular for the food industry several positive examples were mentioned, in which foreign entrepreneurs established well-functioning production and management schemes in the Estonian companies which increased their competitiveness significantly. Other positive examples related to foreign-owned Estonian companies which have a relative high "degree of freedom", so that they can adopt a company strategy specifically targeted to the Estonian situation. On the other hand, however, interviewees reported about examples of food industry companies in which most of the competencies were transferred to the foreign parent company.

As it is shown by the CIS survey from 1998 to 2000 manufacturing branches with greater share of foreign capital are more successful innovators than branches dominated by Estonian owners. In this respect the food industry has an intermediate position since it was estimated in this study that less than 30 % of the food-processing firms are owned by foreign capital, while between 30 % and 49 % of all enterprises are regarded as innovative (Kurik et al. 2002). However, only 16 people were engaged in R&D activities in the food industry in 2000 of which 15 are scientists or engineers (Estonian Institute for Futures Studies 2001). In case of the low technology industries, to which the food industry is counted, acquisition of machinery and equipment are by far the most important innovation expenditures of enterprises, accounting for more than three quarters of all expenditures (Kurik et al. 2002). This fact was highlighted by several interviewees as well, stressing the relevance of machinery purchases for increasing productivity and for meeting technical standards e. g. of the European Union. According to the CIS survey low technology enterprises have a relatively low level of product improvement effects in innovation activities, while process improvements and increasing production capacity have a rather high relevance in these companies. This estimation was only partly agreed on by the interviewees since they stressed that there seems to be a trend of increasing product development activities and capabilities in particular in the Estonian dairy and beverages industry in recent years. In this respect the introduction of specific functional food products (like e. g. probiotic yoghurt, ACE drinks or cholesterol-lowering spreads) were highlighted by several interviewees which seem to have a significant success on the Estonian food market. However, the CIS survey revealed that companies of the low tech industries mainly co-operate with suppliers of equipment or materials as well as clients or customers, but only less than 3 % have co-operations with universities or other research institutions (Kurik et al. 2002). The low relevance of co-operations between research institutions in Tallinn or Tartu and the Estonian food industry was also highlighted during the face-to-face interviews. In addition, there seems to be only very limited interest in Estonian food industry companies to deal with new biotechnological methods, tools or products. This relates in particular to genetically modified organisms.

Wood processing

Estonia's wood-processing industries - like other industrial sectors - underwent a rapid restructuring process in the early 1990s. Currently, the forest and wood-working industries - including primary wood processing, furniture manufacturing and pulp and paper production - are the third largest industrial sector with more than 15 % of total industrial output of Estonia. The share of the wood and furniture industry has increased significantly since the beginning of the 90s (Tiits et al. 2002). The Estonian wood-processing industry is characterised by hundreds of companies, most of them small and medium-sized. The industry employs over 15,000 people of which approximately half of them are in furniture production (Estonian Investment Agency 1999).

The export of wood-based products has considerably increased during the last decade. In 2001, the export of wooden products amounted to 8,566 million EEK (Estonian Trade Council 2002). Estonia has revealed a strong competitive advantage in exports of the wood and furniture industry (Tiits et al. 2002). Main export markets include Sweden, Finland, Germany, the United Kingdom, other EU and European countries and Russia. Like in other traditional industries the wood processing industry of Estonia has attracted considerable foreign investments which are above average of the total manufacturing industry of Estonia (Sinani and Meyer 2002). According to interviewees main reasons for foreign investments are the domestic raw material supply, the highly skilled labour force, moderate wages in the wood-processing industry as well as the market position of Estonian wood-processing companies. Like in other traditional industries foreign-owned firms outperform domestic companies mainly in factors like capital intensity, labour productivity and in the export rate (Sinani and Meyer 2002).

According to the opinion of interviewees there is a considerable trend in the Estonian wood-processing industry to shift the product portfolio in direction of more value-added products. As an example, people highlighted the increasing relevance of production of furniture which was performed by around 230 companies with 7,800 employees in 2001 (Estonian Trade Council 2002). Another indicator in this respect is the result of the recent CIS survey of 1998 to 2000 in which 30 % to 49 % of all manufacturers of wood products, pulp and paper products were characterised as innovators. However, in 2000 only nine employees (of which are seven scientists and engineers) were connected to R&D activities in manufacturing of wood and wood products and additional 35 employees (of which are 16 scientists or engineers) in furniture manufacturing (Estonian Institute for Futures Studies 2001). During the interviews the opinion was raised that wood processing might be a good application industry for modern biotechnology in Estonia in particular in connection with pulp production or to reduce environmental damage with the help of environmental biotechnology. However, there seem to be almost no activities in this area so far and only very limited interest of companies. In addition, most companies of the wood processing industry lack research personnel which is required for internal R&D and innovation activities but also to co-operate with external research institutions.

Environmental technology

According to information given by the interviewed experts there are some relatively small-scaled activities as well as single companies in environmental (bio) technology. Often these companies seem to be of rather small scale but technology oriented. Additionally, a project on biodegradable plastics which was developed at Tartu University achieved relatively high public interest in recent years. It was planned to realise a pilot plant in Põlva to show the feasibility of the concept, but the project is currently stopped due to management problems and financial difficulties. The same relates to a biofuels project in which specific gaz additives on the basis of renewable resources should be developed. In addition, there have been some research and development projects using bioenvironmental approaches to reduce environmental pollution connected to oil shale production and processing. In this context genetically modified micro-organisms have been released in Eastern Estonia around ten years ago. Altogether, there are mainly stand-alone activities in environmental (bio)technology in Estonia so far. Some rather ambitious and promising projects which have been initiated in recent years are currently stopped mainly due to management and financial problems which underlines the specific difficulties in commercialisation of environmental biotechnology experienced also in other European countries.

2.4.2 Regulatory framework of modern biotechnology

The legal framework for modern biotechnology and genetic engineering in Estonia was regarded as being rather favourable both during the interviews as well as expressed in the filled-in data sheets (see chapter 2.1.7). However, interviewees expressed concern that regulation in the biotechnology field might become more bureaucratic, time-consuming and costly after access of Estonia to the EU. In the following a brief overview is given regarding the regulatory framework in the medical field and regarding genetically modified organisms (GMOs) in Estonia.

Regulations in the medical field

Regulation of pharmaceuticals in Estonia is adopted to those of member countries of the EU, in particular to Scandinavian countries. This means that the state controls market approval of pharmaceuticals and has specific registers concerning the approved drugs which are administered at the State Agency of Medicine located in Tartu. In order to get approval for a new drug, a specific dossier has to be submitted to this agency which provides information e. g. about the applicant, production of the drug, preclinical data about toxicity and metabolism of the active substance as well as clinical data mainly concerning efficacy and safety of the drug. In addition, the packaging and the patient package insert have to be delivered to the agency. Similar documents have to be obtained also for market approval of generics but in these cases clinical trial data have to show similarity in the effects of the generic drug with the original pharmaceutical.

In Estonia there is a simplified procedure of recognition for products authorised in the EU by the centralised procedure. Interviewees mentioned in this context that the Estonian authorities generally follow the decisions taken by the European Agency for the Evaluation of Medicinal Products (EMEA), the US Food and Drug Administration (FDA) or national authorities in single EU member countries, Switzerland or Japan. Only in very few cases additional information are requested by the State Agency of Medicine. Most interviewees who had experience with this agency assessed the procedures and the advice given by the agency as adequate although bureaucracy seems to have increased in recent years.

According to interviewees' information clinical trials are regulated in Estonia according to similar rules like in the EU (e. g. informed consent of participating patients, good clinical practice), not least because most international pharma companies which carry out the clinical trials are requesting similar rules like in other European countries. In Estonia, consent has to be given to a clinical trial by the Ethical Committee which includes representatives of all social groups. In addition, the clinical trial has to be approved by the State Agency of Medicine which takes in general two to three months.

Regulations on medical devices in Estonia are based on the rules of relevant EU Directives (such as 90/385/EEC, 93/42/EEC, 98/79/EC). These regulations have been implemented by the Medical Devices Act in 2001. Although the CE mark is not mandatory for a medical device up to now in Estonia, manufacturers or importers of such devices have to show that the essential requirements of related Directives are fulfilled (State Agency of Medicine 2002).

Only some of the interviewees from research institutions and companies had experience with the implementation and practical handling of the regulations related to the medical field. In general, these interviewees expressed the opinion that there are no serious regulatory problems for research or commercialisation of pharmaceutical products or medical devices in Estonia. Most interviewees assess the implemented procedures or practices in this area as "adequate" and the advice given by the State Agency of Medicine as "helpful". Differing views emerged concerning the time requirements taken by the state authorities before coming to a decision: while few interviewees regarded the applied procedures as being too time-consuming, other interviewed experts compared the situation in Estonia with those of other countries and came to the conclusion, that Estonia seems to have an efficient system in this area.

Regulations related to the Estonian Genome Project

The Estonian Parliament passed a specific law titled the Human Genes Research Act on December 13th, 2000 which establishes guidelines for the Estonian Genome Project. The act was put into force in 2001. The target of the law is to facilitate genetic research and regulate the establishment and maintenance of the Gene Bank, and collection, processing and insurance of data. The Gene Bank shall be used only for scientific research into and treatment of diseases of gene donors, public health research and statistical purposes. In addition, it is foreseen that the Gene Bank database shall not be taken outside the territory of Estonia.

According to the Human Genes Research Act participation in the Estonian Genome Project is voluntary and the gene donors' identities are kept confidential. To ensure this regulation the Estonian Genome Project Foundation was established by the Estonian Government in March 2001 which is the legal owner of the database which will be built up within the project. It is foreseen that only a gene donor and the family doctor treating the gene donors shall have the right to receive personalised data. In order to ensure confidentiality of the gene donors, their personal data shall be separated from genetic data. For this purpose each blood sample and set of health data is given a unique 16-digit code (Estonian Genome Project 2002). However, there is a possibility to identify an individual gene donor and his data either on donor's (his family doctor's) request or by the Estonian Genome Project Foundation, in order to acquire additional information about him, following the approval of ethical committee (Sild et al. 2001).

The Estonian Genome Project Foundation acts as interface between single gene donors and researchers interested in the data collected in the database. The Foundation can decentralise operations like accepting the informed consent of potential gene donors, taking tissue and completing health status descriptions to specifically authorised family doctors. However, the Foundation remains responsible for the whole process and cannot delegate certain operations like coding or decoding of the material to third persons (Sild et al. 2001).

Another principle of the Human Genes Research Act is that the gene donor has a right to decide whether to know his gene data or not. If gene donors do not want to participate in the Estonian Genome Project anymore, they have the right to demand deletion of the data that enable identification of the individual person (Estonian Genome Project 2002). In addition, it is foreseen in the act that nobody will be discriminated due to her/his genetic information. Therefore no data shall be issued to insurance companies or employers (Estonian Genome Project 2002).

The interviewed experts regarded the Human Genes Research Act as "progressive" regulation in the field of human genetics and acknowledged that Estonia has learnt a lot e. g. from the experience gained in Iceland. It was seen as crucial for the success of the entire Estonian Genome Project to have a stable legal framework in which researchers can work with the collected data. High priority was given by the experts to ensure the voluntary decision of potential gene donors as well as their anonymity. In this context the problem was highlighted that there might be a conflict between the right to have access to the specific data of an individual gene donor and the general data protection schemes.

Regulations related to genetically modified organisms

In recent years Estonia has adapted its regulations regarding GMOs to those of the EU. In 1999 directive 90/220/EEC was transferred into Estonian law (Act on Conveying of Genetically Modified Organisms into Environment). The Novel Food Regulation of the EU was put into force in Estonia in 2001. In addition, special requirements for labelling of food produced from genetically modified soybeans and genetically modified maize, which are not covered by the Novel Food Regulation, were put into force (Science and Society 2002). The use of genetically modified micro-organisms in contained environments is also regulated according to EU rules.

There are different ministries responsible for the implementation of the relevant EU regulations in Estonia. The Ministry of Environment deals with the implementation of regulations related to the deliberate release of GMOs and market approval. The Ministry of Agriculture is responsible for the Novel Food Regulation, regulations related to seeds and plant reproduction materials, mineral fertilisers and genetically modified animals. Finally, the Ministry of Social Affairs handles regulations related to the use of GMOs in contained environments. In addition, there are two different advisory committees related to GMOs in Estonia:

- Advisory Committee for Genetic Modification (placed by the Ministry of Environment)
- Novel Food Advisory Committee (placed by the Ministry of Agriculture)

Both committees give advice in all questions related to GMOs to the government. In addition, applications for market approval of GMOs are discussed in these committees. So far, two applications of market approval of genetically modified microorganisms have been agreed on by the committees. One deals with a HIV-vaccine which is produced with the help of genetically modified microorganisms. In the other case the approval of genetically modified microorganisms was accepted which shall be used for educational purposes.

Interviewees assessed the regulatory framework related to GMOs as acceptable. However, there was much uncertainty about the practical implementation of the regulations, in particular regarding Novel Food as well as field trials and cultivation of genetically modified plants since there are no activities in this area so far in Estonia. This means that both the administrative bodies as well as the interviewed companies or research institutions hardly have any experience concerning the daily practice of handling these regulations. However, some interviewees expressed the opinion that regulations related to GMOs are handled very flexible and unbureaucratic in Estonia at present, but that the level of bureaucracy might increase after the entry of Estonia into the EU. Currently, problems arise in controlling and testing a potential contamination of food, feed and seed with genetically modified material. This is partly due to lack of established control methods and certified laboratories in Estonia, partly due to uncertainties and lack of agreement in international committees dealing with these questions (e. g. about the allowed contamination level in seeds).

2.4.3 Public acceptance of biotechnology

So far, there has been no intensive public debate on genetically modified organisms or novel food in Estonia. According to information given during the interviews there are regularly some articles related to this topic in public newspapers or on television, but the debate is regarded as being rather fact oriented than emotional. In addition, it was stated that the Estonian population has high confidence in the scientists active in this field. The relatively low public interest in GMOs was explained by the lack or rather low research activities and commercial activities in this area in Estonia.

The Ministry of Environment conducted a survey at the end of 2001 in order to analyse the acceptance of genetically modified food and agricultural products in Estonia. Around 90 % of the respondents did not have enough information related to this topic and wished to get more information. This opinion was in particular widespread among the Russian population of Estonia. Only 6 % of the interviewees felt themselves well informed. Related to the acceptance of genetically modified food and agricultural products a high level of uncertainty was revealed in the survey. 40 % of the respondents answered that they do not have a specific opinion on this topic. Another 31 % did not support the use of GMOs, while 6 % were in favour of such organisms.

The relatively low intensity of the public debate related to GMOs in Estonia was further explained by the limited influence of the environmental movement as well as the low presence of environmental organisations such as Friends of the Earth or Greenpeace in this country. Some interviewees expressed the opinion that the environmental movement has gained relevance in recent years in Estonia, but the organisations active in this field do not concentrate their activities on GMOs.

Another point in the public debate in the last few years was the establishment of the Estonian Genome Project Foundation as well as the details of the shaping of the Human Genes Research Act. According to information given by the interviewees there was a relatively small public debate in press and television related to this topic. During this debate no fundamental criticism or strong religious or ethical arguments have been raised against the project, but the discussion was focused on specific questions in order to ensure the security of the collected genetic data. Several interviewees expressed the opinion that there are opponents against the Estonian Genome Project, but often they do not express their opinion in public. In addition, there is no organised criticism or opposition against this project so far.

The initiators of the Estonian Genome Project conducted three population surveys in order to analyse acceptance of such an activity. The first survey revealed that around 6 % of the population did not accept the project. On the other hand, only 40 % of the citizens of Estonia felt informed about this activity. The third survey indicated that now around 60 % of the population felt adequately informed about the project, while the acceptance rate did not change. The Estonian Genome Project Foundation tries to inform the population via public media (e. g. television, broadcasting, public press), specific information brochures as well as a telephone or e-mail hotline about the targets and details of the project. In general, the benefits of the project are highlighted during these information activities as well as its impact on progress and development of Estonia. Despite the general positive attitude in the population related to the Estonian Genome Project, the organisers currently have difficulties to collect the required blood samples. While it was planned to collect around 10,000 samples during the pilot phase until 2003, there are only a few hundred blood samples available so far. The organisers of the project explained this fact with problems during the certification process of the family doctors who are collecting the samples. In addition, the filling-in of the required questionnaires of the blood samples donors is rather time-consuming and has to be done by the family doctors as well. The relatively high acceptance of the project expressed in the population surveys is explained partly by the legal framework of the Human Genes Research Act which aims at securing safety of the data, ensuring strict anonymity of the blood donors as well as preventing genetic discrimination of blood donors, e. g. by employers or insurance companies. Several interviewers regarded the Human

Genes Research Act as "best international practice" in providing a legal framework for human genome projects. According to several interviewees there was a relatively intensive debate between representatives of biotechnology companies, research institutions and legal advisors, while drafting this law. However, there was only very limited opposition in the Parliament as well as almost no public debate related to this topic afterwards.

Several organisations initiate activities in order to inform the public about modern biotechnology. In addition to information material provided e. g. by the Ministry of the Environment, the Academy of Sciences, several research institutions and the Estonian Genome Project Foundation are active in this respect. Furthermore, there was an essay competition sponsored by a big private bank in which students should express their views to the problems and benefits of modern biotechnology. However, most of the initiators of such activities reported about a limited interest of the general public and low participation of the "ordinary citizens" or other target groups. In conclusion it can be stated that acceptance of modern biotechnology is no "hot topic" in Estonia so far, but people lack information in this respect. Some interviewees stated that additional initiatives should be taken to discuss the framework conditions of the application of modern biotechnology in Estonia, in order to prevent an "explosion" in the public debate related to this topic like it occurred e. g. in the Mediterranean countries at the end of the 1990s.

2.5 Strengths, weaknesses and future development of the innovation system

Both specific strengths as well as some bottlenecks for the future development of biotechnology in Estonia can be identified from the analysis of the biotechnology innovations system in this country. During the interviews as well as in the subsequent analyses, the following aspects emerged as specific strengths of the biotechnology innovation system in Estonia:

- Well-defined internal networks of the main scientific and commercial actors in biotechnology in Estonia which facilitate the realisation of scientific projects and commercial activities.
- Substantial amount of research activities in the biomedical field in Estonia which are strongly interlinked with research groups in other European countries.
- Sufficient availability of qualified staff at least in the core disciplines related to biotechnological research.
- Increasing interest of students in the field of life sciences and informatics.

- Certain commercialisation activities in particular in the biomedical field resulting in a relatively high number of biotech companies in relation to the population in Estonia.
- Adequate legal framework in the medical field and related to genetically modified organisms.
- With the Human Genes Research Act Estonia has established one of the first regulations in the field of human genetics world-wide and created a stable legal framework in this area.
- User-friendly implementation and application of the specific regulations related to biotechnology.
- Favourable general infrastructure and entrepreneurial climate in Estonia (e. g. tax system with specific advantages for companies, low bureaucracy, liberal economic policy).

According to the analysis of the different fields of the biotechnology innovation system in Estonia the main bottlenecks for the future development of biotechnology in this country are existing in the following areas:

Knowledge base/skills network

- Lacking funds for interdisciplinary research.
- Subcritical R&D capacities and activities in application areas of biotechnology outside the biomedical field.
- Availability of scientific infrastructure (like equipment pools and laboratory space), in particular in the Tallinn region and in Tartu outside the biomedical field.
- Low interest of high school students in science and engineering studies.
- The needs of potential user industries of biotechnology (e. g. pharmaceutical, chemical, food industry, wood processing) are not adequately considered in the current academic education of students. The same relates to the integration of biotechnology-related management and business aspects in the scientific education.
- Technical staff often is not educated in modern biotechnological methods and techniques and trained with up-to-date laboratory equipment.

Industry/supply network

- Lack of or missing availability of technical infrastructure and up-to-date and expensive scientific equipment (e. g. for genome sequencing or proteine analysis, high-standard safety laboratories, high-speed Internet links) both for research activities in the biotechnology field as well as commercialisation activities of scientific findings.

- Public and private services and support in IPR issues and business activities (like general management techniques, marketing, distribution or production management) related to dedicated biotechnology companies.
- Vocational training in modern biotechnology techniques both for scientific and technical personnel.
- Low awareness of personnel development issues in biotechnology companies and traditional user industries.

Finance/industrial development network

- The very short-term perspective of existing investment schemes and expectations of potential investors do not meet the requirements of biotechnology companies.
- There is almost no investment capital for the seed phase of a biotech company available in Estonia.
- Lack of general instruments for business financing due to the low interest of private banks or other financing institutions.

Market/social acceptability network

- In most biotechnology companies there is a low awareness and lack of experience related to marketing needs as well as management options in this area.
- Awareness of potential traditional user industries (e. g. food, chemical and wood-processing industry) of the benefits and potentials of innovative technologies in general and modern biotechnology in particular.
- The absence of Estonian R&D-oriented pharmaceutical companies impedes the domestic commercialisation of scientific findings in the biomedical field.
- Small domestic market in Estonia and in consequence the need to access international markets also for young and small-scaled companies which often lack specific knowledge on the situation and development of international markets as well as marketing and adequate business strategies.

Trajectories of the innovation system

In order to have a kind of reference system for the future development of the biotechnology innovation system in Estonia, some insights are given concerning the development of this system within the coming years, in case no specific activities and new initiatives are realised. When analysing these "future trajectories" of biotechnology in Estonia, it has to be taken into account that no quantitative forecasting methods can be used, due to the limited number of actors as well as the short time frame for which data are available. However, some likely future developments can be outlined based on general considerations of the linkages between the different networks of the Estonian biotechnology innovation system.

Without specific initiatives and policy actions by the Estonian Government rather scattered and stand-alone activities can be expected on the research level and in the commercial field related to biotechnology in Estonia. Due to the already existing contacts and their experience in acquiring EU funds, it seems most likely that Estonian researchers in the biomedical field will increasingly link their own research activities in networks with research groups with similar or complementary competencies in EU and other candidate countries. However, since so far there is no (European) experience with the new European funding instruments (networks of excellence and integrated projects) there seems to be some risk in extrapolating previous success in acquiring European funds to the new framework programme. In contrast, the development of future co-operations within Estonia is regarded rather sceptically, in particular between the bio(techno)logy-oriented scientists in Tartu and the engineering disciplines at Tallinn Technical University, due to the limited budgets available for this purpose, the general difficulties of co-operations between differing scientific disciplines and the "existing competition" between the two locations. Outside the biomedical field (e. g. agro-food, plant biotechnology, environmental biotechnology, bioprocessing), research activities most probably will be limited to single researchers or small working groups in the coming years. Without specific initiatives to further develop the knowledge base of non-biomedical research in Estonia, researchers in these fields will face increasing difficulties to compete successfully with their biomedical colleagues for the Estonian research budgets since they have a restricted "track record" and less developed contacts to researchers in other European countries.

On the commercial level it seems most likely that by far the majority of the existing specialised companies in the biomedical field will show moderate growth in the coming years. The growth potential of these companies is impeded by their low business orientation, the risk-averse attitude of the company owners and the lack of knowledge and experience in management and marketing techniques of company founders and managers. The few biomedical companies with an explicit business orientation (which often are able to attract venture capital or the interest of wealthy private investors) most probably will show higher growth rates in the coming years, but their growth potential is limited mainly due to lack of financial resources and the rudimentary developed venture capital, private business financing opportunities and capital market in Estonia. The success of the commercialisation activities of the Estonian Genome Project cannot be foreseen at this stage, but the suggested strategy of EGeen Ltd. implies a high degree of risk and requires a substantial amount of investment capital as well as a mid- to long-term time horizon. Furthermore, it seems most probable that at least part of the benefits – in case the strategy can be successfully realised – will not be allocated to Estonia. Outside the biomedical field the very few existing Estonian biotechnology companies will face specific difficulties due to the restricted domestic market and the restricted export opportunities in other European countries.

Given their low interest in innovations in general, it does not seem very realistic that potential user industries (e. g. food, chemical, wood-processing industry) will take up new biotechnological methods and techniques to a substantial extent in the coming years in Estonia without specific initiatives in this direction. In the pharmaceutical field the potential application industry is almost lacking in Estonia at the moment. Taking into account the current trends of mergers and acquisitions as well as co-operation agreements between multinational pharmaceutical and specialised biotech companies, only single (if any) buying-in-activities of international pharmaceutical or biotechnology companies into Estonian companies should be expected in the coming years. Altogether, a relatively limited impact of biotechnology on the overall Estonian economy in terms of employment, production and exports can be expected in the coming years without specific initiatives as suggested in chapter 4 of this report.

The major challenges for the future development of the biotechnology innovation system in Estonia relate to substantiate the research activities in the biomedical field, to build up the management and marketing skills of the company founders and managers in this area, to develop the research activities in the non-medical fields of biotechnology, to awake the interest of the traditional industries in innovation and modern technologies in general and biotechnology in particular, to improve the co-operative climate between biotechnology-related disciplines and locations within Estonia, as well as to further develop the financial instruments, and the capital market for high-tech industries in Estonia.

Access of Estonia to the EU

The forthcoming access of Estonia to the European Union most probably will not result in serious short-term changes related to the biotechnology innovation system within this country. Most of the existing EU regulations in the biotechnology or medical field already have been transferred to Estonian law. During the interviews the impression arose that the different regulations are implemented in a relatively user-friendly and non-bureaucratic way in Estonia which slightly might change after EU membership of the country.

Furthermore, scientists of Estonia active in the biotech field already participated to a high extent in research programmes of the EU or dedicated calls of the European Commission specifically targeted to candidate countries. In this sense it seems unlikely that the participation and acquisition of funds by Estonian scientists will extensively increase after the EU access of Estonia. But often this step the country can participate in specific structural or regional funds of the EU which will amount to substantial sums. Whether biotechnology related research or commercial activities will profit from such developments is primarily a question of the priority setting within the Estonian Government and the rules set up by the EU for the use of these funds. Given the high priority which innovation activities, also in the biotech field, have in the current Estonian policy (as e. g. highlighted in “Knowledge-based Estonia”), it seems rather likely that positive impacts will arise for the Estonian biotechnology innovation system, in particular related to research funding, building up of scientific infrastructure, education activities and public (co)financing of innovation activities in this field.

After access of Estonia to the EU export of products and services also related to biotechnology will be facilitated into other EU member countries. However, the interviewed representatives of the Estonian biotech companies did not report about significant regulatory hurdles for such activities, but more about problems related to marketing and distribution, which will not be significantly influenced by the access of Estonia to the EU. With regard to the application industries, the food industry will face the challenge to fulfil the EU hygiene and environmental standards within a relatively short time frame which will require substantial private and public investments in this area.

With respect to the financial markets, the interests of international investors in Estonian biotech companies the commercialisation of scientific results as well as the general economic policy, no significant short-terms effects with direct relevance for biotech companies are expected from the access of Estonia to the EU, since there have been low restrictions for financial transfers into and outside of Estonia in recent years. Depending on the exact conditions of the EU entry of Estonia, some interviewees expressed misgivings that the Estonian Government might decrease specific tax advantages for companies and that bureaucracy might increase in general. Taken all together, it should not be assumed that the attractiveness of Estonia as an biotech location will significantly increase just due to the EU access of this country.

3. Benchmarking of the innovation systems

In the first part of this chapter a qualitative benchmarking of the Estonian biotechnology innovation system against the respective systems of Austria, Finland, Germany, Ireland and the UK is made. For this exercise the four compartements of the innovation system concept as described in chapter 2 are used as analytical framework. The second part of the benchmarking is based on a set of quantitative indicators for scientific and commercial performance.

3.1 Qualitative benchmarking

The qualitative benchmarking is organised within the four compartments of the biotechnology innovation system of Estonia. In each compartment the specific strengths and weaknesses of the situation in Estonia form the basis for the benchmarking against the reference countries.

Knowledge/skills network

Biotechnology draws on a number of different disciplines. Increasingly not only the "classical" science base (like biology, chemistry and medicine) fuels into biotechnolgy but also disciplines like informatics, mathematics, materials research and not least social sciences. In order to build up a competitive knowledge base for biotechnology these and other disciplines need to be integrated into biotechnology research. Since science traditionally is organised along disciplines it is rather difficult to establish a real interdisciplinary organisation of biotechnology-related research. This can be observed in most of the reference countries and also in Estonia: We find a certain lack of interdisciplinarity in biotechnology although the scientific and commercial actors active in the biomedical field are well interlinked with each other in Estonia. On the science side, Estonian researchers active in biomedicine are also already incorporated in rather advanced networks with research groups in other European countries. However, this does not apply to the same extent to networks with researchers of other disciplines inside and outside of Estonia.

In principle interdisciplinary research projects could be funded by the Estonian Science Foundation and also as targeted research projects by the Ministry of Education in Estonia. But no specific incentives or initiatives have been realised to motivate researchers of differing disciplines to jointly carry out scientific projects in this country so far. In some of the reference countries specific efforts have been made recently to improve the situation. For example in the UK the research councils support networking between different disciplines. In Germany an interesting new programme on systems biology was set up with the explicit target of promoting interdisciplinary research. If applying for grants from this programme it is not sufficient to claim the application of an interdisciplinary approach. Rather it is necessary to provide sound track records. This means that researchers from biology, engineering sciences and mathematics/informatics need to be part of the research team. Such a programme approach requires also that special evaluation criteria for interdisciplinary projects are developed and that evaluation panels are set up who include the required interdisciplinary experience.

Biotechnological concepts and tools are increasingly used in various research areas thereby opening new strategies for research. Internationally the biomedical field is most advanced in this respect. The Estonian situation is not different from other countries and in terms of interaction between biotechnology and biomedical research compares well with the reference countries. However in other areas, in particular in food and nutrition-related research and chemical research, biotechnology has not been able yet to exert substantial impact in Estonia. This situation is different from most of the reference countries. Although, in principle, the Competence Centre Programme of the Ministry of Economic Affairs and Communication could be a tool to improve the links between biotechnology and traditional user industries, it seems rather unrealistic that such a development will occur in the coming years since most companies of these industries have low interest in R&D and innovation activities and therefore did not build up the necessary in-house capacity and expertise to co-operate with scientific institutions. In particular in those countries with a strong research tradition in biotechnology the integration of biotechnology with such traditional application areas is well established. The situation in Estonia could be compared with the Irish situation some years ago. Ireland faced similar problems as Estonia today in particular in the food sector. In order to improve the situation, food research centres were enabled to receive additional funding for biotechnology research. Furthermore, a special agency was set up to manage these efforts.

Not least the international human genome sequencing projects impressingly illustrated that modern biotechnology increasingly relies on large scale and expensive equipment such as automatic sequencers, lab robots, NMR and mass spectrometers. To make such equipment accessible for interested users from research organisations is a challenge for any country developing a modern biotechnology research base. In this sense, the situation in Estonia is not different from this general situation. However, in Estonia regional and sectoral differences could be observed in a sense that the availability of scientific infrastructure is a particular problem in the Tallinn region and in the Tartu area mainly outside the biomedical field. No specific initiative from Estonian state institutions has been suggested so far to renovate laboratory space or to buy up-to-date scientific equipment in the life science field in Estonia. To improve the situation setting up centres providing such infrastructures has been a common strategy in several countries: in Germany central facilities have been set up for genome research, in Finland biocentres also provide access to equipment pools and in the UK a Joint Research Equipment Initiative tackles this problem.

Biotechnology with its strong knowledge intensity requires highly qualified and skilled personnel. In addition, the very dynamic scientific development of biotechnology calls for a general capability of continuous learning of the involved personnel. Starting at high school education the interest in science and engineering seems to cease in many of the reference countries and also in Estonia during the last years. Awareness campaigns targeted at schools have been initiated in some countries in this context including for example special information programmes with practical demonstration of biotechnology or also specific seminars and workshops for school teachers. Single Estonian interviewees reported that awareness campaigns in high schools have been initiated in Estonia as well in order to increase interest of high school students in engineering and science studies.

The availability of skilled technical staff and the requirement for vocational training in biotechnology are other critical factors for the functioning of any biotechnology innovation system. In particular due to the growing "technisation and automatisation" of biotechnology and also its increasing maturity the demand for qualified technical staff is expanding internationally. This is a problem in particular in those countries where the biotech industry is well developed. However, also in Estonia already today problems are arising in this field. It seems that vocational training in general has a low image in Estonia. In addition, from the side of the state there is no clear strategic orientation towards the needs of industry. On the other hand, industry itself does not seem to invest adequately in vocational training and personnel development of employees. However, no specific programme or adequate solution was found for this problem in the reference countries so far.

Concerning universities matching academic education and the needs of user industries is another general problem of biotechnology which could concern for example specific skills for life sciences such as bioinformatics but also the integration of economics and management courses into biotechnology curricula. There is a sufficient availability of staff in the core disciplines of biotechnology and the interest of students in biotechnology seems to increase in Estonia. However, the match between higher education and the needs of industry seems to be worse compared to the reference countries. In Estonia, so far no specific political initiative tackles this area. The better situation in the reference countries may be due to the fact that various measures have been taken in these countries to improve the situation. For example in the UK the Teaching Company scheme provides specific funds for placing graduates in a company to work on a specific project supervised by academia and industrial researchers thereby trying to improve the integration between academia and industrial needs. Another approach in the UK is the Science

Enterprise Challenge which provides financing for so-called enterprise centres in universities. These are centres that teach entrepreneurship and business skills in the science and engineering curricula. Thereby they train, develop and support the people who will make new knowledge- based ventures successful. The centres' activities combine educational activities and mentoring of new ventures and entrepreneurs at early stages of development. They operate throughout the home university and usually have partnerships with the local business community. In addition strategic international alliances are built by such centres. The Company Campus Programme in Ireland run by Enterprise Ireland should be mentioned as a third initiative aiming at improving the combination of biotechnology research with economic skills,. This programme is designed to assist individuals to commercialise R&D on the college campus. It provides assistance to researchers interested in commercialising R&D and helps academic entrepreneurs to assess the commercial viability of their innovative technologies. Support is given in the form of business development advice, financial assistance, mentoring facilities and specifically designed part time business training courses.

Industry/supply network

Not only for research institutions but also for companies access to technical infrastructure and modern and expensive equipment (such as instruments for automatic sequencing or protein analysis, safety laboratories, high-speed Internet links) is an important asset. Compared to the reference countries the situation of the Estonian biotechnology industry is unfavourable in this respect. This may be due to the early stage of the industry, the difficulties to raise venture capital funding which could be used for such investments as well as the pure focus of Estonian science park initiatives to provide only space for new or established companies. In some of the reference countries special care has been given to equipment and technical infrastructure when setting up technology parks in a sense that these parks provide such equipment and also offer technical support and maintenance by the park management.

The creation of biotechnology firms is mostly based on scientific discoveries, new methodological approaches or the combination of existing but so far not connected knowledge. In most cases scientists with an academic background are the driving forces for company foundation. Only rarely new companies arise as spin-outs from existing companies. Since academic founders usually are not experienced in business and management issues (in particular in handling IPR issues), lacking knowledge in these areas makes business and market orientation of new companies often rather difficult. In Estonia lacking market and business orientation of biotechnology companies seems to be a larger problem than in the reference countries although e. g. in the context of the SPINNO programme attempts are made to increase awareness of potential company founders in this respect. In most of these countries specific measures have been taken to provide the required business information and support for new biotechnology firms. For example in Finland the biocentres provide support in IPR issues, management and marketing. In Austria TECMA (technology marketing Austria) was founded as an organisation with the task to exploit patents. It supports the commercialisation of research results from Austrian universities, companies and private individuals by licensing and selling inventions and know-how. In Germany a specific project (INSTI) has been launched by the Federal Ministry of Education and Research in the mid 1990s which provides SMEs with access to the scientific technical information gathered in patents documents and in addition specific patent information centres were established. In Ireland the Company Campus Programme also aims at providing the required business support to academic spin-outs.

Biotechnology is not an established industry sector and internationally there exists only a limited number of biotechnology companies (approximately between 4,000 and 5,000 in the year 2001 according to a recent Ernst & Young survey) which per se exert only limited economic impact in terms of employment, revenues or external trade. However, biotechnology bears the potential to improve the economic situation of a number of traditional user industries by supporting the development of new products and services which could create new markets and the introduction of new processes which could improve competitiveness of companies. At present these indirect effects of biotechnology can already be observed in the pharmaceutical sector. It is expected that the chemical and the food sector will follow this example. In Estonia we observe rather weak links between such user industries and biotechnology. In contrast, the coupling between biotechnology and user industries is well developed, in particular in the pharmaceutical sector, in all reference countries. In other sectors analogous links are just emerging. With respect to the pharmaceutical sector there are differences in the adoption rates of biotechnology. The USA and the UK started earlier to take advantage of biotechnolgy. However, in particular Germany caught up since the mid 1990s. Various measures have been taken in these countries to improve the adoption of biotechnology by user industries. For example in Germany and Ireland direct support to these industries was given for doing biotechnology-related research. In the UK the so-called BIO-WISE initiative provides a whole set of measures for solving such problems. The programme not only gives advice to traditional industries how to use biotechnology but also supports the development of the biotechnology supplier industry. It provides independent advice through help-lines and a website, free publications describing benefits of using biotechnology, free visit to SME from an industrial biotechnology specialist, grant support to companies to demonstrate the benefits of biotechnology, information and advice to biotechnology suppliers and free events that present biotechnology in action and provide opportunities for networking.

Finance/industrial development network

Important factors shaping the general entrepreneurial climate of a country include for example the corporate tax system, the level of bureaucracy relevant for business activities and the general orientation of economic policy. With respect to these factors Estonia compares favourably with the reference countries. Estonia provides a positive general entrepreneurial climate for biotechnology which could be compared with the situation in Ireland, where these general factors were main driving forces for the development of high-tech industries including biotechnology during the last years.

Biotechnology is not a short-term endeavour. The development of products and also new technologies in biotechnology is a time-consuming activity. Return from financial investment cannot be expected in a short-term. Rather a medium or long-term perspective is needed. Compared to the reference countries current financing schemes and views of investors in Estonia are characterised by a very short-term perspective, which makes the development of medium-term oriented and sustainable business strategies rather difficult if not impossible.

An important factor for creating a viable biotechnology industry is the availability of seed financing for early stages of company development. Compared with the reference countries such seed capital is widely lacking in Estonia and no political initiative tackles this area so far. In contrast in most of the reference countries seed financing programmes have been implemented in recent years: the University Challenge in the UK, the seed financing programme in Austria, SITRA seed funds in Finland, seed initiative of Enterprise Ireland and public seed financing programmes in the USA. The SITRA experience seems most interesting for Estonia since it provides smart money, aims at building up strategic alliances with other investors and brings in experience with financing other technologies so that a broad technology experience can be provided.

Financing of biotechnology business does not only rely on venture capital. Rather common instruments for private business financing (such as credits, loans, leasing opportunities) are frequently used in the reference countries. In Estonia, however, such common instruments are rarely available not only for biotechnology companies but also for other industries. This could also be related to the early stage of high-tech industry financing in a sense that financing institutions have no experience with higher risk businesses and are not used to be engaged in such industries. Drawing on experience in other countries measures to increase awareness of established financing institutions about opportunities in biotechnology seem to be advisable.

Market/social acceptability network

At the current international state of biotechnology main target markets for biotechnology firms are not markets for consumer goods, but often they aim at public organisations such as universities or research institutions that buy biotechnology equipment and supplies. Another target group of biotech companies are established user industries from the pharmaceutical and increasingly the chemical and food sector which procure pre-products such as drug candidates, process and technology know-how and also information such as databases from biotechnology firms. In Estonia such user markets are rarely developed at the moment. In particular there is no domestic pharmaceutical sector and the established user industries in the chemical and the food sector so far do not seem to be interested in biotechnology. Therefore a general international orientation of biotechnology business in Estonia is a must and in addition the creation of a domestic user market in particular in the chemical and food sector seems to be advisable.

The regulatory framework for biotechnology is largely determined by EU guidelines and directives which are implemented at a national level. Due to this European harmonisation there are only minor national differences in the setting of the regulatory framework. Rather, national peculiarities relate mainly to the way how regulations are handled and implemented. In Germany and Austria for example complex and time consuming implementation procedures had been a problem for industrial activities in the 1990s. However, streamlining such procedures and providing additional funds for staff for regulatory authorities helped to improve the situation in Germany considerably while in Austria there are discussions about introducing additional regulatory hurdles. The regulatory framework for biotechnology in Estonia can be assessed as favourable in the European context. Estonia has transferred all relevant EU directives into national laws and pursues an user-friendly strategy for the implementation of these rules. As a particular strength of Estonia the Human Genes Research Act should be mentioned which provides a stable legal framework for modern human genetics research which is not yet existing in the reference countries.

3.2 Performance benchmarking

Indicators which are used for the quantitative benchmarking are summarised in table 3.1.

Table 3.1: Indicators for benchmarking the biotechnology innovation systems

Indicator	Unit	Estonia		Austria		Finland		Germany		Ireland		UK	
		Value	Rank	Value	Rank	Value	Rank	Value	Rank	Value	Rank	Value	Rank
Scientific performance													
Biotechnology publishing intensity 1990-1995	Publications/mio capita	30.77	6	150.96	3	298.56	1	138.52	4	115.27	5	208.72	2
Biotechnology publishing intensity 1996-2001	Publications/mio capita	143.47	6	415.11	3	658.22	1	340.91	4	297.72	5	478.68	2
Biotechnology publishing growth	Growth rate 2001-1996/1990-1995	366%	1	175%	2	120%	6	146%	4	158%	3	129%	5
Biotechnology publishing intensity 1996-2001	Publications/1,000 researchers	55.85	6	179.27	2	140.63	4	114.81	5	150.05	3	189.95	1
Significance of biotechnology 1991	% biotech publications/total publications	1.74	6	3.97	2	4.75	1	3.46	5	3.51	3	3.48	4
Significance of biotechnology 2001	% biotech publications/total publications	4.81	6	8.19	2	8.68	1	7.55	4	7.89	3	7.47	5
Life sciences publishing intensity 1990-1995	Publications/mio capita	517.21	6	1451.36	3	2999.31	1	1422.23	4	1156.60	5	2801.64	2
Life sciences publishing intensity 1996-2001	Publications/mio capita	727.66	6	1957.26	3	3377.85	1	1660.54	4	1505.07	5	2838.45	2
Life sciences publishing growth	Growth rate 2001-1996/1990-1995	41%	1	35%	2	13%	5	17%	4	30%	3	1%	6

Table 3.1 continued

Indicator	Unit	Estonia		Austria		Finland		Germany		Ireland		UK	
		Value	Rank	Value	Rank	Value	Rank	Value	Rank	Value	Rank	Value	Rank
Commercial performance													
Specific number of biotechnology firms in 2000	Number of firms/mio capita	7.62	3	7.27	4	14.88	1	4.01	6	8.19	2	4.60	5
Specific vc invested in biotechnology 1996-2000	PPP$/capita	3.80	4	0.30	6	5.83	3	9.78	1	2.11	5	6.49	2
Specific field trials GMO 1996-2000	Notifications/mio capita	0.00	6	0.37	5	3.49	1	0.99	4	1.08	3	1.94	2
Biotechnology patenting intensity 1990-1995	Patent applications/mio capita	3.97	6	24.51	2	29.90	1	21.99	4	9.58	5	23.27	3
Biotechnology patenting intensity 1996-2001	Patent applications/mio capita	2.58	6	25.03	4	27.43	3	32.33	1	21.27	5	32.31	2
Biotechnology patenting intensity 1996-2001	Patents/1.000 researchers	1.00	6	10.81	3	5.86	5	10.89	2	10.71	4	12.82	1

Source: Fraunhofer ISI 2002

Scientific performance

Considering biotechnology publishing intensities for the two periods 1990 to 1995 and 1996 to 2001 related to population size of the country, the benchmark is set by Finland which is followed by the UK, Austria, Ireland, Germany and Estonia. A different picture emerges if we include the dynamics of biotechnology publishing intensity. Now Estonia sets the benchmark indicating a considerable growth of biotechnology publishing intensities during the 1990s. If publishing activities are related to the number of researchers, the United Kingdom shows up to be the best performing nation followed by Austria, Ireland, Finland, Germany and Estonia. Looking in more detail at the Estonian performance for publishing intensities in biotechnology, the rather low amount of gross expenditure in R&D in Estonia seems to be one of the reasons for the performance pattern. If publishing intensities are related to GERD, Estonia ranks far ahead of all other countries which is due to the very low GERD. In other words, low expenditures on R&D have been a limiting factor for the development of research activities in Estonia during the 1990s.

The significance of biotechnology measured as percentage of biotechnology publications in total publications is highest in Finland for both periods considered, followed by Austria, Ireland, the UK, Germany and Estonia. The only alteration which took place between the two periods is that Germany and UK changed places. It also becomes obvious that in all countries biotechnology gained significance during the 1990s. However in Estonia, biotechnology has not yet achieved the weight in the research community as can be observed in the other countries.

Publication intensities in life sciences related to population reveal the same pattern as publication intensities in biotechnology: again the benchmark is set by Finland followed by the UK, Austria, Germany, Ireland and Estonia. The similarity between both life sciences in total and biotechnology in particular seems to indicate that a broad life science base provides a good starting point for the development of biotechnology. In all countries growth in life sciences' publishing intensities could be observed during the 1990s. The benchmark for growth rates is set as in biotechnology by Estonia indicating a very dynamic development during the 1990s.

Commercial performance

Considering the specific number of biotechnology firms in 2000 Estonia ranks at the third place among the compared countries. Obviously, Estonia has already succeeded to build up a considerable number of biotechnology companies, in particular if the small size of the country is taken into account. As indicated by the specific venture capital invested in biotechnology at least some of these companies perform well in the European comparison in terms of attracting venture capital investment. Estonia ranks at the fourth place for this indicator. The benchmark is set by Germany which is not surprising because during the second half of the 1990s

Germany developed to the most attractive country for biotechnology venture capital in Europe.

In terms of specific field trials with genetically modified plants Finland is performing best among the compared countries, followed by the UK, Germany, Ireland, Austria and Estonia which had no field trial notification during the period considered. This seems to indicate that the commercial development of the agro-food biotechnology sector in Estonia has not yet proceeded far. There have been only few European biotechnology patents filed by Estonian actors during both periods considered. Therefore, in terms of biotechnology patenting intensities related to population or related to researchers, Estonia ranks at the end of the compared countries. Finland, Germany and the UK are setting the benchmarks for these indicators.

Taken together, the benchmarking of the Estonian biotechnology innovation system against Austria, Finland, Germany, Ireland and the UK allows the following conclusions:

- In terms of scientific performance Estonia has been behind these countries during the 1990s by most measures applied. However, it is remarkable that Estonia is performing best among all these countries in terms of growth of scientific performance. Obviously, a very dynamic process has started in Estonia.
- Looking at commercial performance Estonia is doing well in terms of number of biotechnology firms and venture capital invested. However, it has to be taken into account that the entire venture capital was invested by one venture capitalist in only two biotech companies. In addition, the relatively weak performance in terms of patenting intensities at the European level seems to indicate that the technological basis of the Estonian biotechnology industry may face some difficulties in an international competition.

4. Recommendations

The Estonian biotechnology sector started to grow out of its infancy. Many research institutions act in international networks. The industrial sector is budding in terms of SMEs that start to interact in the international arena. However as the benchmarking against some of the more mature biotechnology innovation systems in Europe has shown, the critical mass which is required for developing a sustainable biotechnology sector has not yet been achieved in Estonia. There exists a number of obstacles for the commercial exploitation of biotechnology in Estonia. This applies to all compartments of in the innovation system. Starting from the results of the benchmarking, the following chapter will outline recommendations for shaping the knowledge and skills network, in particular related to research institutions and the education sector, it will give hints to strengthen the commercial sector and will delineate financing measures and activities to improve the framework conditions.

4.1 Overall strategy

In order to fully exploit the commercial potential of biotechnology in Estonia a dual approach is recommended aiming at both, to develop biotechnology as an important field in the high-tech sector and as tool to increase innovativeness of the economicly more relevant low- and medium tech sectors.

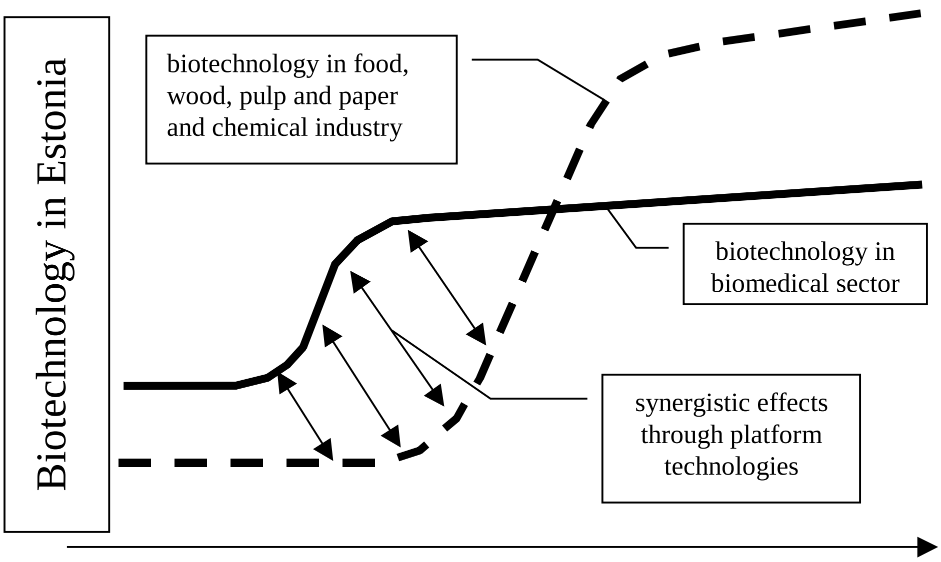
At present the biomedical field is dominant within the biotechnology sector in Estonia. Most internationally competitive research activities are found in this sector and spin-off activities take place mainly with biomedical background. An important boost for further implementation might be the Estonian Genome Project, although the commercial success of this project cannot be foreseen at the moment. However, Estonia lacks medium-sized and large pharmaceutical companies that could be a customer for the products of the biomedical spin-off companies. Therefore the markets for these companies have to be approached abroad.

Although it can be expected that dedicated biotechnology companies will grow in the coming years in Estonia, their impact on the national economy in terms of employment, turnover generated and exports will remain limited given their current starting position. In addition it seems unlikely that existing Estonian pharmaceutical companies or international pharmaceutical companies will commercialise drug candidates in Estonia so that the overall impact of the biomedical field on the Estonian economy will be limited in the coming years. Therefore it is suggested to realise a strategy which tries to expand biotechnology related innovations to other application fields as well.

The so-called low- and medium tech industries like food processing, wood processing and the chemical industry are important factors in the Estonian economy. At present these sectors lack the awareness of need of innovations. We propose within a medium- to long-term strategy to strive for achieving a tighter coupling between biotechnology and these industries and thereby facilitate the introduction of the innovative capacity of biotechnology into the above mentioned sectors. This will improve the competitiveness of Estonian industry and the applicable biotechnology research.

The dual stage master plan of *Biotechnology Implementation into Economy* allows synergistic effects between the biomedical sector, which is already advanced in scientific and technical terms, and the low tech industries. This will allow to miss out the initial establishing problems in the low tech industries. Additionally it can be assumed that the two stage strategy allows partly the external financing of otherwise internal costs. Figure 4.1 illustrates the dual stage master plan for biotechnology in Estonia.

Figure 4.1 Dual stage master plan for biotechnology development in Estonia



A second general part of the overall strategy concerns policy co-ordination. The problem is well known: innovation is a systemic, horizontal phenomenon caused by and influencing a broad spectrum of factors, while the related political institutions are quite narrowly and vertically in their thematic focus, working departmentalised and fragmented. These discrepancies, nevertheless, are becoming one of the most serious bottlenecks of future innovation systems. Therefore, putting more emphasis on co-ordinated policy approaches for supporting the Estonian biotechnology innovation system in the future including policy implementation at the level of ministries and agencies can be defined as a more generic task which will be crucial for success. In particular activities of the Ministry of Education and the Ministry of Economic Affairs and Communication to support biotechnology innovation require co-ordinated efforts not only at the level of ministries but also at the level of the operating agencies which are responsible for implementation.

4.2 Recommendations to improve the research sector

4.2.1 Structural measures

Estonia has reached a kind of critical mass in the field of biomedical research. Further improvement of efficiency of biomedical research could be achieved by incentives for co-operation. This should comprise both co-operation between different faculties (biology-medicine; biology-physics; biology-engineering) and inner Estonian co-operation between related institutes in different regions (especially Tartu-Tallinn). For example closer co-operation activities in the field of cancer research on an epidemiological and molecular level between the Estonian Institute of Experimental and Clinical Medicine, KBFI, the Institute of Molecular and Cell Biology at Tartu University, the Medical Faculty and the University Clinic Tartu could be of specific interest.

Measures:

- To improve interdisciplinary research we suggest that the Estonian Science Foundation should set aside a specific budget for interdisciplinary projects (for all application fields of modern biotechnology, but also other scientific disciplines) in which participants must prove that different scientific disciplines from different faculties are integrated into the proposed research. This means that it is not sufficient to claim interdisciplinary. Rather it is necessary to provide track records. An integral part of such a programme is the development and use of special evaluation criteria for interdisciplinary projects and also the setting up of evaluation panels who possess the required interdisciplinary experience.
- Additionally the Centre of Excellence Programme of the Ministry of Education should be shifted towards interdisciplinary research. Since the first phase of the programme just has been finalised it is recommended to carry out an interim evaluation of the impact of the programme and the results achieved at the selected Centres. For the second phase of the programme stronger emphasis should be put on interdisciplinarity, i. e. financing of researchers participating in

such Centres should be connected to their willingness to participate in sound multidisciplinary projects with a clear scientific focus.

To achieve sustainable development in biotechnology research, infrastructures of research institutions (especially lab facilities, equipment) in particular in the Tallinn region should be updated. This should apply to both core biotechnology research institutions and to biotechnology-related disciplines such as engineering, chemistry, development of bioanalytical devices (optics, micro-electronic). These sectors should also be increasingly connected to biomedical research in interdisciplinary research projects (see above).

Measures:

- We suggest to integrate a new infrastructure initiative into the future biotechnology programme where in a first step the existing needs in the different biotechnology domains are identified by the research communities in the main locations (Tallinn and Tartu) and in a second step funds are provided for updating infrastructures in individual groups but also for establishing central facilities (for example for sequencing or protein analysis) in the two locations which could be used by all research groups who are in need of such equipment. Additional activities related to modernise and maintain scientific infrastructure and equipment are foreseen in the suggested science and technology parks (see chapter 4.3.1), and in the programme for facilitating adoption of new biotechnologies in units of agro-food and chemical-related research (see chapter 4.2.2).

4.2.2 Development and adjustment of R&D capacities in user sectors in Estonia

Research capacities in the biomedical sector are adequate to pursue the short-term high-tech development of biotechnology. In contrast the integration of biotechnology into low tech sectors requires an adjustment of R&D resources. In order to support the utilisation of biotechnology in such user industries, we propose to take advantage of the Irish experience in this context where a centre approach was pursued.

Measures:

- Set up a specific programme for facilitating the adoption of new biotechnologies by research units in the agro-food and chemical sector. Such a programme should encompass funding for joint projects between such units and research groups from universities and other research institutions that can bring in biotechnology competencies. A second part of this programme should provide funds for modernising infrastructure and equipment in the sector research units.

The suggested programme could be part of the Competence Centre Programme of the Ministry of Economic Affairs and Communication. It is neither possible nor necessary to engage in all disciplines related to biotechnology such as engineering in detail. However, it should be guaranteed that education and research allow at least networking activities in the underrepresented research areas with experts from abroad.

- Improve university education at the interface between established technologies in user industries and modern biotechnology (see following chapter).

4.2.3 Recommendations for higher education

At present higher education is mainly focused on the academic career. To introduce aspects of industrial relevance into university curricula and in general to raise the awareness of commercial opportunities and business perspectives of bio-research a set of different additional measures and new initiatives is recommended which draws on the experience in Ireland with the Company Campus Initiative and in the UK with the Science Enterprise Challenge.

Measures:

- Following the Science Enterprise Challenge example of the UK we propose to provide financing for so-called enterprise centres in universities that teach entrepreneurship and business skills in the science and engineering curricula. They should also provide mentoring of new ventures and entrepreneurs at early stages of development. Building up partnerships with the local business community and setting up strategic international alliances are additional tasks of these centres.[10]
- External experts from industry should take part in the teaching activities at universities.
- Additionally industrial internships could be compulsory during the bachelor course.
- A public scholarship programme could be issued to send students to internationally accepted schools for economic master programmes.
- As outlined Estonia will have to focus its business activities at least in the biomedical sector on markets outside Estonia. Though in general English language skills of students seem to be rather good, teaching in English could facilitate the internationalisation of education. In a longer perspective this could also help to attract foreign students to Estonia, who might be future co-operation

---

10 Activities within the SPINNO programme which have been already started at Tallinn Technical University and with the BIOSPINNO initiative aim in the suggested direction.

partners. Under the same point of view the arrangement of summer schools in biotechnology could favour future co-operations.

4.2.4 Recommendations for vocational training

In order to improve the availability of technical staff for biotechnology research institutions and companies in Estonia we suggest the following new

Measures:

- To develop and implement a national curriculum for the education of technicians in biotechnology and the relevant application areas of biotechnology. Besides biotechnology there could be curricula for technicians in food technology, agriculture, medicine, physics, mathematics and others.
- As a first step of the development of the curricula representatives of research institutions, biotechnology firms and user industries should elaborate the basic requirements of the curriculum taking into account the international developments. A draft framework for essential parts of the curriculum is presented in table 4.1. During the stakeholder workshop it was highlighted that some activities already have been started in Estonia to develop national curricula for technicians.

Table 4.1: Essential contents for new curricula of vocational training in sectors related to biotechnology

orientation	**essential contents for curricula**
biotechnology	basic genetic engineering techniques, sequencing, handling of laboratory automation equipment, novel analytical techniques for biotechnology, cell and tissue culture, bioprocessing
food technology	food processing, microbiology, fermentation technology, basic gene technology, GMP regulations
agriculture – plant biotechnology	gene technology, modern plant breeding techniques, GMP regulations
medicine	animal testing, basic gene technology, GMP regulations
physics	optics, handling and limitations of biological material, measurement instrumentation
mathematics	statistics, basics in biology

4.2.5 Research and innovation financing

The share of biotechnology in the overall (relatively restricted) budget for R&D in Estonia seems appropriate although the total budget for R&D activities in Estonia is regarded as being too small. However, it should be assured that enough money is dedicated to basic research in the biomedical and non-biomedical field and that resources are focused and not diverted into too many sub-critical efforts.

The initiatives and instruments used by ESTAG in order to stimulate innovation activities in research institutions and companies were generally appreciated by the interviewees. The application procedure was perceived as "demanding" but could be realised with reasonable efforts using the support provided by ESTAG. However, most of the interviewees criticised the evaluation process and the time requirements of the ESTAG procedures. Therefore it seems advisable that ESTAG incorporates independent, international scientific and technical experts in the evaluation of project proposals exceeding a financial volume of 1 million EEK. In most cases those experts can give recommendations about cost and economic aspects of such a proposal as well. Since the evaluation of the procedures of ESTAG and the needed time requirements have not been the target of this study[11], no recommendations are given in this respect.

4.2.6 Framework conditions for research

Framework conditions for research seem favourable in Estonia. Though the Human Genes Research Act is said to be very progressive it seems necessary to prove its suitability for foreseeable future developments.

Measures:

- From a data protection perspective we suggest to re-evaluate the exact procedures, the future handling of data and the guaranteed personal accessibility before the commencement of the major project phase of the Estonian Genome Project.

[11] Another specific project dealt with these aspects which was finalized in 2002.

4.3 Recommendations to improve the industry sector

4.3.1 Science and technology parks

Science and technology parks for fostering the commercialisation of biotechnology have been set up in many countries and also in Estonia the park concept has been adopted. International experience has shown that science parks per se cannot guarantee commercial success and that benefits for tenant companies (such as intensive interaction with the host university or access to business services) can be limited. Potential problems of science parks comprise (too) high ground rents, pre-disposition of tenant companies to co-operate only with the host institution even if external institutions might be more relevant, and lacking or inadequate innovation support. Success factors for science parks include a continuous monitoring of the needs of tenant companies, the forging of links to funding organisations and private financiers, the provision of training programmes for technical staff and entrepreneurs and the promotion of links between host university and tenant companies. Based on the analysis of the present situation in Estonia and on international experience a stronger co-ordination of the various initiatives in Estonia (Tartu Science Park, Tartu Biotechnology Park, Biotechnology and Incubation Centre in Tartu, technology park initiative in Tallinn, incubator facilities in Tallinn) under sectoral aspects seems advisable. Otherwise the science parks will compete for tenants and existing synergistic effects to other tenants and/or research institutions are wasted. In order to further develop the science/technology park concept we suggest the following

Measures:

- Concentrate efforts on two science parks for life science related activities that however should be equipped with the main analytical scientific instruments (such as sequencing machines, NMR and mass spectroscopy), infrastructure in telecommunication (high-speed Internet links etc.) as well as with the standard laboratory equipment such as ultracentrifuges.
- The equipment should be pooled and technical support should be offered by the park management.
- The necessity of a safety laboratory for genetic engineering should be checked with potential customers of the park. Taken into account the research activities in Estonia it seems important to construct at least one or two high-safety laboratories that can be rented by the tenants on demand.
- Other support such as financing, book-keeping and advice in intellectual property rights should be provided on a professional basis. Since it can not be excluded that the needed professionals would prefer to set up their own business

it is recommended to manage the interface to external experts (by making available contacts to relevant experts) as an alternative to integrating such services into the park itself. The selection of recommended experts should be done by the park management according to quality criteria.

- From a networking perspective the science and technology park should have meeting- and conference rooms and associated presentation facilities.
- Additionally sound arrangements are recommended with potential financing institutions as soon as possible to ensure the actual realisation of the science and technology park idea. This includes arrangements concerning the financial commitment of initiating institutions.
- Taking into account the already running initiatives and already existing science and technology parks as well as the potential demand of existing and newly founded companies, it seems advisable to concentrate the efforts in Tartu in one initiative which incorporates all three activities running in this region and tries to develop a financially sound concept rather short-term which offers specific equipment and service activities in order to be attractive for biotech companies. In Tallinn a life science related park concept should be developed in the framework of the general technology park initiative. Due to the very limited availability of up-to-date laboratory space and equipment in Tallinn, it seems necessary to plan a new building for this purpose in which interested companies and research institutions can use the facilities. Therefore the realisation of such a concept in Tallinn might take more time than in Tartu.
- The state or other public institutions (e. g. regions, cities) should take an active role in co-ordinating the running activities as well as (co-)financing the purchase of scientific equipment.

4.3.2 Access to the market

The analysis of the situation of Estonian companies showed that many companies lack the awareness of market demands. Both marketing strategies and marketing activities are underdeveloped in the overall business strategy of most biotech companies.

Measures:

- We suggest to start measures to raise the awareness of biotech SMEs for these topics. Measures could include seminars about marketing for entrepreneurs e. g. initiated by ESTAG and the consideration of marketing aspects in relevant curricula in the scientific and engineering higher education.

- On the other hand public institutions such as the Estonian Innovation Agency should boost their activities in joint marketing activities abroad, e. g. on trade fairs or special road shows in selected countries.

Lacking awareness of innovation needs among user industries (in particular food and chemical industry) limits market potentials for biotechnology companies and also endangers the competitiveness of these industries. In order to improve this situation and increase the awareness for potentials of biotechnology we propose two different initiatives. The first one is a set of different measures according to the experience made in the UK with the BIO-WISE programme.

Measures:

- Set up a new initiative by ESTAG that provides independent and free information for traditional industries on how to use biotechnology in order to increase competitiveness. Advice could be provided via helplines, publications, personal visits of industrial experts, organisation of events. For maintaining this service funds for independent industry specialists would be required.
- Provide grants for demonstration projects via ESTAG where companies can show benefits of using biotechnology.

The second initiative is a public technology procurement instrument where policy places an order for a certain product or service that does not exist at the time but which could be developed within a reasonable period. Technology development is required to meet the demands of the public procurer. Procurement needs not to be restricted to completely new products or services it could also be applied for the adaptation of certain products to specific needs. Thereby applying new technology can be stimulated among traditional sectors. In particular we propose the following procurement activity:

Measures:

- The Government (e. g. the Ministry of Economic Affairs and Communication together with the Ministry of Social Affairs) should place an order for new or improved products which can be developed with the help of modern biotechnology. The precise definition of the order should be elaborated together with experts from all application areas of biotechnology. Such an activity would fit well into the portfolio of Enterprise Estonia.

The protection of their intellectual property rights as well as improving market introduction and marketing of biotech-related products and services are among the most important future challenges of Estonian biotech companies. However, both activities are one of the core interests of private companies and private entrepreneurship. Therefore, public authorities should improve the framework conditions in this field but should rarely intervene directly in these processes. In addition to practical problems (e. g. which patent applications of biotech companies should be supported by public activities), EU regulations set narrow limits in this field. Therefore, it is recommended that Estonian authorities try to improve the financing situation of biotech companies (see chapter 4.4), in order to enable them to finance patent applications (also for international patents) as well as marketing activities by their acquired financial resources.

4.4 Recommendations to improve finance/industrial development

The main problems related to business financing in biotechnology are the lack of medium or long-term financing options and a lack of suitable financing schemes for the early start-up phase of companies. In order to improve the situation we propose to establish a seed fund taking into account experience made with SITRA in Finland.

Measures:

- We suggest to establish a special seed fund for high technology companies with an initial volume of 108 million EEK. Biotechnology should be a focus of the fund but it should also invest in other high technology areas. In order to manage investments in a competent way the biotechnology part should be managed by two life sciences specialists. The fund should take a minority stake in the company not exceeding 40 % of the company's equity so that full responsibility lies with the entrepreneur. The size of the investment depends on the specific requirements of the company. We expect a range of 3 million EEK to 15 million EEK per investment. Average duration of investments should be for at least five years. Funding should be smart in a sense that management and business support is provided by the fund. In this context establishing international contacts to investors and customers plays a crucial role. Therefore it is important that the fund establishes an international network through links with other investors. As a starting point it seems advisable to build up contacts with SITRA in Finland and to explore the possibility of taking advantage of SITRA support in implementation of such a fund and its management.
- The suggested seed fund should be regarded as a starting point for (semi-)public activities in order to improve the financing situation of biotech and other high-tech companies in Estonia. In this sense it should be taken into account that additional activities might be necessary in the coming years in order to facilitate the increasing financing needs of fast growing companies.

4.5 Summary and implementation plan

The proposed Estonian biotechnology strategy comprises a set of measures to improve the situation in three areas:

1. Knowledge base
2. Education
3. Commercial development

For these areas the following measures are proposed, the suggested time frame for the various initiatives is summarised in table 4.2. The proposed strategy should be implemented during a five years period:

1. Knowledge Base:

- Set up a specific programme for interdisciplinary research in life sciences by the ESF.
- Provide specific funds for updating scientific infrastructures.
- Set up a programme for supporting the adoption of biotechnology in agro-food and chemical research units including funds for modernising infrastructures.

The proposed measures to support the biotechnology knowledge base should be implemented as soon as possible because they create the required preconditions for commercial development. In order to improve mid-term orientation and planning security a time frame of five years for these activities is recommended.

The total costs of this part of the programme are estimated to 99 million EEK for five years. About 48 % are planned for interdisciplinary research, 28 % for updating scientific infrastructure, and 24 % for the biotechnology adoption measure.

2. Education

- Establish business education centres at universities.
- Set up an education programme providing grants for international scholarships.
- Introduce industrial internships into master programmes.
- Develop and implement a modern curriculum for education of technicians.
- In addition interest of high school students for science and engineering should be improved by e. g. initiating awareness campaigns at schools.

These measures should be implemented within the coming five years. Since experience tells that modifications of educational systems take rather long times it is recommended to start the initiative rather soon. The business education centre initiative should start about one year after commencement of the total programme.

Total costs for the education sub-programme are estimated to about 8.5 million EEK for five years. 44 % would be devoted to business centres (two centres, one in Tartu and Tallinn each), 54 % to financing scholarships (five per year) and 2 % to developing and implementing the technicians curricula.

3. Commercial development

- Establish two science parks related to life science activities, one in Tartu and one in Tallinn.
- Build up information programmes on marketing and business strategies for biotech SME.
- Set up a programme informing traditional industries about biotechnology potentials and providing advice for adoption.
- Set up a procurement initiative for the development of new or improved products based on modern biotechnological methods and tools.
- Set up a seed capital fund for high technology start-ups.
- Initiate a round table for established financing institutions in order to increase awareness for high technology financing.

The commercial initiative should start at the beginning of the programme because it implies a number of planning processes that require a certain period of time.

Costs for the commercialisation programme for five years are estimated to about 250 million EEK with the lions share of about 46 % going to the science parks and another 43 % to the seed capital fund. SME information would require about 0.5 %, the adoption programme around 2 %, and the procurement initiative 8.5 %.

On this basis the total costs of the programme are estimated to about 357 million EEK for five years.

The proposed biotechnology strategy for Estonia tackles a broad variety of different individual functions of the innovation system starting from high school education and ending at international marketing of Estonia. This strategy can only be successful if the various initiatives are implemented in a co-ordinated way. In other words, success requires a balanced policy mix, focusing just on individual measures without taking care of their systemic context will most likely result in sub-optimum outcomes.

Table 4.2: Time frame for the implementation of the Estonian biotechnology Strategy. "Short-term": implementation at the start of the initiative "Medium-term": implementation about 1 – 2 years after the start

Measures	**time-frame**	**comment**
1. Knowledge base		
Programme to support interdisciplinary research	short-term	
Funds for scientific infrastructure	short-term	
Support adoption of biotechnology in agro-food and chemical research	short-term	
2. Education		
Business education centres	medium-term	
Grants for international scholarships	short-term	short-term start and mid-term implementation
Industrial interships in master programmes	short-term	short-term start and mid-term implementation
New curricula for technicians	short-term	takes time to implement, therefore short-term start recommended
Awareness campaigns for life science and engineering at school	short-term	takes time to implement, therefore short-term start recommended
3. Commercial development		
Science parks in Tartu and Tallinn	short-term to medium-term	Tartu biotech science park to start immediately, Tallinn biotech science park needs some more time for preparation
Information programmes on business issues for biotech SME	short-term	
Programme to inform user industries about biotechnology and support adoption	short-term to medium-term	planning to start as soon as possible since implementation takes more time
Procurement initiative	short-term	placement of procurement as soon as possible, implementation can proceed during the whole five years according to milestones.
Seed capital fund	short-term	
Round table for financing institutions	short-term	

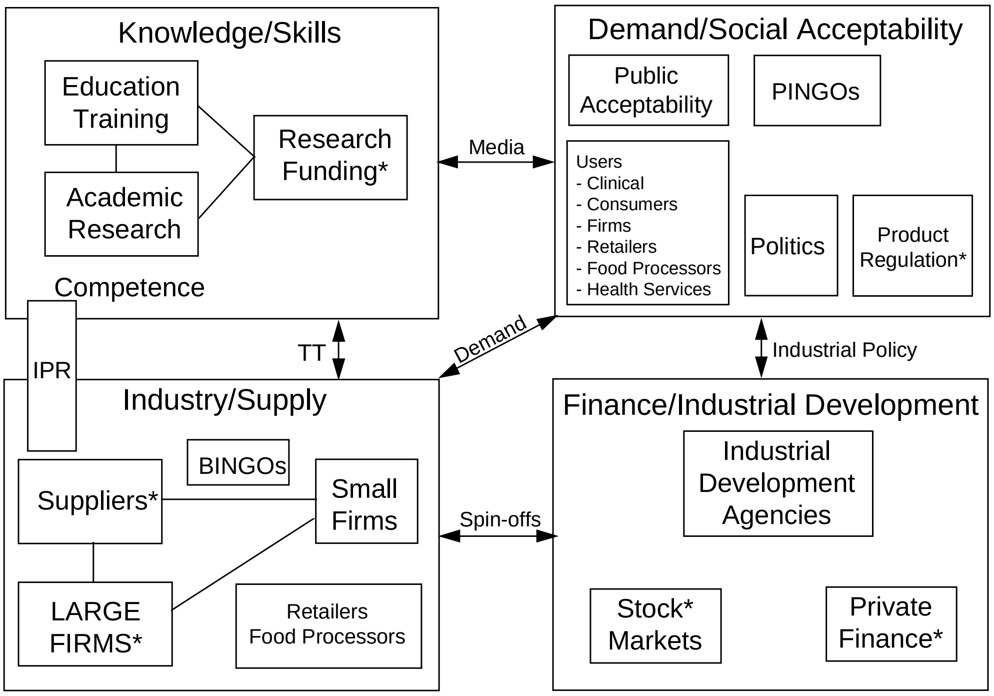
Annex

A1 Methodology and working steps

One of the central outcomes of modern innovation research is the finding that innovations do not follow a linear path from basic research to applied research and further to industrial development and market introduction of new processes and new products (e. g. Edquist 1997, Lundvall 1988, Kline and Rosenberg 1986). Instead, innovation activities are characterised by complicated feedback mechanisms and interactive relations, involving science, technology, learning, production, policy and demand. In consequence, commercial companies almost never innovate in isolation, but they interact with "organisations" of different types (e. g. suppliers, customers, research institutions, investment companies, government agencies) and their behaviour is also shaped by "institutions" (Edquist 1997) which constitute constraints or incentives for innovation (e. g. laws, cultural or social rules, technical norms).

Due to their complex character, innovation activities represent an ideal area to use system theory approaches for the analysis of such processes on the level of the national economy (e. g. Lundvall 1992, Nelson 1993, Edquist 1997). Therefore, the concept of the project is designed in such a way that the interaction between the different actors and influential factors, which are regarded as being significant to innovation, can be considered in the study. Figure A1.1 gives a simplified overview of the factors relevant to innovation networks, in which the relevant institutions and organisations are embedded as well as their interrelationships. The main components of the framework of the study are the networks of knowledge and skills, industry and supply, demand and social acceptability as well as financing and industrial development of biotechnology in Estonia.

Figure A1.1: Network of key factors influencing innovation in biotechnology



*International influence

BINGOs = Business interest non-governmental organisations
IPR = Intellectual Property Rights
PINGOs = Public interest non-governmental organisations
TT = Technology Transfer

Source: Senker et al. 2001

The following working steps have been carried out within the project:

- Analysis and mapping of the biotechnology innovation system in Estonia
- Analysis and mapping of the international development of biotechnology
- Interim report
- Benchmarking of the Estonian biotechnology innovation system with selected countries
- Elaboration of recommendations for policy actions
- Providing of a final report

A1.1 Biotechnology innovation system in Estonia

The target of this working step is the analysis of the biotechnology innovation system in Estonia. For this purpose quantitative data and qualitative information are collected for all aspects decisive for this innovation system. As outlined in figure A1.1, this includes information on the networks of key factors influencing innovation. The following data have been collected and analysed during this working step:

- Knowledge/skills network:
  - Structures and activities of R&D institutions related to biotechnology
  - Structure and development of research funding related to biotechnology
  - Education and training possibilities
- Industry/supply network:
  - Structure and development of dedicated small biotechnology companies
  - Structure and activities of large multinational companies
  - Structure and development of industrial fields relevant for the exploitation of biotechnology-related products and processes
- Finance/industrial development network:
  - Existing innovation support policies, structures and services
  - Private funding possibilities of biotechnology companies
  - Rules and functioning of the capital markets
  - Public policies to support innovations and the creation of start-ups in the field of biotechnology
- Demand/social acceptability network:
  - Conditions and development of markets relevant to biotechnology
  - Expectations and acceptance of biotechnology in potential user groups
  - Legal framework for product approval or other market-relevant regulations

Actor-oriented approach to analyse the innovation system

In a first step the project team of Fraunhofer ISI analysed available studies and reports concerning the structure and specific aspects of the innovation system in Estonia. For this purpose the Ministry of Economic Affairs and Communications of Estonia provided information about already existing studies which were complemented by database and internet searches by Fraunhofer ISI. The project team collected the identified articles or reports (e. g. from the EU, OECD) and analysed them according to the different networks relevant for the biotechnology innovation system in Estonia. In addition, available statistics and documents relevant for the legal framework of biotechnology and its application industries were screened by the project team.

An important element to collect the required information of the project were face-to-face interviews analysing the structure and activities of biotechnology companies, research institutions, service providers (including administrative agencies and financing institutions) and policy-makers in the biotechnology field in Estonia. Before developing specific interview guides as well as data sheets for each group, telephone interviews with four members of the expert committee (scientists, representatives of companies, policy administration) were carried out covering topics like the general framework conditions of biotechnology in Estonia, relevance of scientific and commercial activities outside the biomedical field, relevance and activities of the pharmaceutical industry as well as the financing and regulatory situation of biotechnology companies in Estonia. The information given during these telephone interviews were included in the development of specific interview guides and data sheets for research institutions, biotechnology companies and service providers. Draft versions of the interview guides and data sheets were transferred to the Ministry of Economic Affairs and Communications of Estonia at the beginning of October 2002 who forwarded them to the members of the expert panel. The suggestions of the experts were included in the different interview guides and data sheets by the project team of Fraunhofer ISI in the second week of October 2002. The final versions of these documents were transferred to the Ministry of Economic Affairs and Communications on October 14th, 2002.

The interview guide for biotech companies includes questions related to the business activities of the company, the assessment of the policy framework in Estonia, co-operation activities, financing of the company, education and training possibilities, the conditions and development of relevant domestic and international markets, the legal framework in Estonia, intellectual property rights issues as well as suggestions for policy actions. In the data sheet mainly quantitative figures are requested related to the business activities and financing of the company, co-operation activities as well as some innovation output parameters.

The interview guide for research institutions includes questions related to the research activities of the institute, the assessment of the policy framework in Estonia, co-operation activities, education and training possibilities, the conditions and development of relevant domestic and international markets, the legal framework in Estonia, intellectual property rights issues as well as suggestions for policy actions. In the data sheet additional quantitative figures are requested related to the personnel and financing of the institute, co-operation activities as well as some innovation output parameters and technologies used.

The interview guide for service providing companies or financing institutions includes questions related to the targets and activities of the institution, the assessment of the policy framework in Estonia, the character of the service activities, instruments for financing of high-tech enterprises (in case the institution is active in this field), education and training possibilities, the conditions and development of relevant domestic and international markets, the legal framework in Estonia, intellectual property rights issues as well as suggestions for policy actions. In the data sheet additional data are requested related to the personnel and financing of the institution and co-operation activities.

In order to prepare a first round of personal interviews, the project team of Fraunhofer ISI screened publicly available data sources (like e. g. internet pages of companies, research institutions or service providers, international biotechnology guides, participants in EU research programmes) as well as internal documents provided by the Ministry of Economic Affairs and Communications for the addresses of biotechnology and pharmaceutical companies, research institutions and service providers. A list of institutions in the Tallinn area (consisting of 10 companies, 6 research institutions, 10 service providers) was sent to the Ministry of Economic Affairs and Communications at the beginning of October 2002. In the following weeks the Ministry arranged meetings for personal interviews with representatives of the different groups. The interviewees were informed about the target and working programme of the project. The data sheet as well as the interview guide of the respective group were forwarded to the interviewees around one week before the interview in order to give them an opportunity to prepare the interview and collect the required data. In addition, they were asked to fill in the data sheet before the interview.

In the week from October 21st, 2002 to October 25th, 2002 a total of 18 face-to-face interviews (with representatives of four biotechnology companies, one pharmaceutical company, six research institutions, two financing institutions, two ministries, one business association and one law office) were carried out by a member of the project team of Fraunhofer ISI. The developed interview guides proved to be suitable for the topics relevant for the project. The data sheets were filled in by 12 of the 18 interviewees before or after the interview. Interestingly all interviewed companies filled in the data sheet.

A second round of interview was carried out in the week from November 18th, 2002 to November 22nd, 2002 by four members of the project team of Fraunhofer ISI. In order to prepare these interviews, a list of additional 13 institutions in the Tallinn area (mainly research institutions, financing institutions or service providers), 33 institutions in the Tartu region (mainly biotechnology companies and research institutions) and additional six other institutions was prepared by Fraunhofer ISI at the end of October 2002. During this week a total of 37 face-to-face interviews were carried out by the project team. These included representations of biotechnology companies, research institutions and service providers. Details concerning the interviewed persons and their institutional background are given in table A1.1. A total of 55 face-to-face interviews were carried out in the frame of this project. 31 of the contacted institutions are located in the Tallinn area and 22 institutions in the Tartu region.

Table A1.1: Interviewed persons during the project

Person	Institution	Type of institution
Eek-Piirsoo, Liina	Ministry of Environment, Tallinn	Ministry / Administration
Engelbrecht, Jüri	Estonian Academy of Sciences / Research Competence Council, Tallinn	Research institution
Heinaru, Ain	Tartu University, Department of Biology and Geography, Tartu	Research institution
Järvik, Ivar	Kevelt, Tartu	Biotechnology company
Järviste, Jüri	Estonian Small Business Association, Tallinn	Business association
Kaldalu, Andrus	Asper Biotech + Biodata, Tartu	Biotechnology company
Kaldmäe, Hedi	Mikrotaim - plant biotech company, Räpina	Biotechnology company
Kamratov, Ardo	Tallinn Technical University's R&D Department, Tallinn	Technology transfer institution
Karis, Alar	Visgenyx, Tartu	Biotechnology company
Kattel, Rainer	Tallinn Technical University, Public Administration and Innovation Policy, Tallinn	Research institution
Kivi, Tarmo	Baltic Small Equity Fund, Tallinn	Financing institution
Kivikangur, Kristel	Farma, Tallinn	Pharmaceutical company
Kogerman, Kristjan / Kogerman, Priit	InBio, Tallinn	Biotechnology company
Kotkas, Katrin	Estonian Plant Biotechnical Research Centre EVIKA, Saku	Research institution
Kruuv, Kirsta	Estonian Genome Project, Tartu	Research institution
Kubo, Kitty	Ministry of Economic Affairs and Communications, Tallinn	Ministry / Administration
Kuiv, Anti / Kangro, Igor / Luik, Argo / Pralla, Illmar	ESTAG, Tallinn	Ministry / Administration
Kumar, Jüri	Estonian Agrobiocenter, Tartu	Research institution
Lepmets, Taavi	LHV, Tallinn	Financing institution
Lopp, Margus / Siirde, Kaarel	Prosyntest, Tallinn	Biotechnology company
Lukas, Tauno	Ministry of Agriculture, Tallinn	Ministry / Administration
Maimets, Toivo	Institute of Molecular and Cell Biology, Tartu	Research institution
Metspalu, Andres	Estonian Genome Project Foundation, Tartu University	Research institution
Mikelsaar, Aavo Valdur	Labas, Tartu	Biotechnology company

Table A1.1 continued

Person	Institution	Type of institution
Mikelsaar, Marika / Saatre, Jane	Tartu University Institute of Microbiology, Tartu	Research institution / technology transfer institution
Mölder, Erki	Quattromed, Tartu	Biotechnology company
Nõlvak, Rainer	Celecure, Tallinn	Biotechnology company
Nymann, Roland	Estonian Plant Production Inspectorate, Saku	Ministry / Administration
Olevsoo, Vevo	Estonian Chamber of Agriculture and Commerce, Tallinn	Business association
Paalme, Toomas	Department of Food Processing of Tallinn Technical University, Tallinn	Research institution
Pärna, Ott	Ministry of Economic Affairs and Communications, Tallinn	Ministry / Administration
Pikani, Jaanus	Egeen International, Tartu	Biotechnology company
Puurand, Ülo	Iasgen, Tartu	Biotechnology company
Samoson, Ago / Kogerman, Priit	National Institute of Chemical Physics and Biophysics, Tallinn	Research institution
Sarap, Margus	Käosaar & Co, Tartu	IPR advice
Sarkovski, Aleksander	Tartu Universiy, Institute of Pharmacology, Tartu	Research institution
Schults, Olev	Cresco, Tallinn	Financing institution
Siigur, Urmas	Tartu University Clinics, Tartu	Research institution
Sild, Tarmo	HETA, Tallinn	Law office
Sirendi, Meelis	Estonain Science Foundation, Tallinn	Financing institution
Sutrop, Margit	Tartu University Center of Ethics, Tartu	Research institution
Tasa, Andrus	Tartu Biotechnology Park / Bioincubation Centre, Tartu	Technology transfer institution
Teesalu, Tambet	Applied Phenomics, Tartu	Biotechnology company
Terk, Erik	Estonian Institute for Futures Studies, Tallinn	Research institution
Toots, Indrek	NAXO, Tartu	Biotechnology company
Truve, Erkki	Department of Gene Technology of Tallinn Technical University, Tallinn	Research institution
Ustav, Mart	Tartu University Institute of Technology, Fit Biotech, Tartu	Research institution / technology transfer institution / biotechnology company
Vaikmäe, Rein	Ministry of Education, Tallinn	Ministry / Administration
Vanatalu, Kalju	CDN, Tallinn	Biotechnology company

Table A1.1 continued

Person	Institution	Type of institution
Veidebaum, Toomas	Estonian Institute of Experimental and Clinical Medicine, Tallinn	Research institution
Viirg, Andrus	Estonian Investment Agency, Tallinn	Ministry / Administration
Villems, Richard	Estonian Biocenter / Bioincubation Centre, Tartu	Research institution
Vilosius, Toomas	Estonian Parliament, Tallinn	Ministry / Administration
Vilu, Raivo / Tüksammel, Ove	Proekspert, Tallinn	Biotechnology company

The developed data sheets include information on the general and innovation activities of the company or institution, staff, financial aspects, assessment of the framework conditions, and on networking activities. Prior to the interviews, the data sheets were sent to all interview partners. 15 data sheets were sent back by companies, seven by research institutes and five by service providers. The statistical analyses were performed with SPSS Version 11.0 for Windows and with Microsoft Excel 97.

Methodology of bibliometric and patent analysis

Complementary to this actor-oriented approach an output-oriented methodology was used to investigate the scientific and technical activities and the specialisation profile of biotechnology in Estonia. For this purpose bibliometric and patent indicators for Estonia and the benchmarking-countries were worked out by the project team of Fraunhofer ISI.

Bibliometric and patent analyses were carried out in order to gather internationally comparable data supporting the benchmarking of Estonian biotechnology activities. Bibliometric and patent indicators were constructed as they are seen as the most important indicators representing results of research and development (R&D). However, both indicators reflect the activities of different phases of the innovation process. While scientific publications, which are the basis for generating bibliometric indicators, are generally seen as representing the output of basic research activities, patents represent the output of applied research and technological development. For the present study we generated time series of publication and patenting activities in order to reflect development trends. Data from 1990 onwards was gathered and will be presented. The analysis was based on a definition of biotechnology using the classification schemes of the databases used in combination with key words.

Publication data was retrieved using the Science Citation Index (SCI). The online version of the database offered by the host STN was used as data source. The SCI is one of the largest international multidisciplinary databases. It covers more than 5,000 scientific and technical and medical journals. The SCI is widely used for international comparative analyses and evaluation exercises.

In order to be able to assess the importance of biotechnology research in Estonia and the benchmarking countries, in addition, we retrieved publication data for the life sciences in general and calculated the share of biotech publications, respectively. The life sciences were delimited using a definition offered by the SCI. The SCI, as offered by the host STN, can be divided into six data base segments. One of those segments is restricted to the life sciences and was used for delimitation.

Patent analysis was based on the analysis of international patent data. Only patent applications applied for at the European Patent Office were used[12]. Considering only European patent applications (Grupp and Schmoch 1999), provides internationally comparable data avoiding the effects of the so-called "home advantage", which has to be taken into consideration if patent data from national patent offices would be used. Using international patent data guarantees that the patents applied for have to meet the same requirements for being granted, the patenting procedure and the legal framework are identical for all patent applications. This also results in the fact that – with a few exceptions – only high quality patents with a propensity to be commercially exploited are taken into account as the international patenting procedures are rather costly (Schmoch 1999). Patent data was retrieved using two different patent databases provided by the host Questel, EPPATENT and WOPATENT. The first containing all patent documents applied for at the European Patent Office (EPO) and the latter those applied for through the PCT[13] procedure.

For both, the bibliometric and the patent analysis, not only data for Estonia was retrieved, but also for the countries considered in the benchmarking exercise: Germany, the United Kingdom, Finland, Ireland and Austria.

Based on the publication data a specialisation profile of Estonian research activities was calculated. Due to the low numbers of patent applications, we omitted calculating a specialisation profile for the more applied Estonian R&D activities.

---

[12] Patent applications in the area of biotechnology were identified based on a field delimitation using IPC (International Patent Classification) Codes. The following codes were used: C12M,C12N,C12P,C12Q,C12S,A61K-039,A61K-048,C02F-003,G01N-027/327,G01N-33/53?,G01N-033/54?/IC,G01N-033/55?,G01N-33/56?,G01N-033/57?.

[13] PCT = Patent Cooperation Treaty. The PCT procedure was introduced in 1978 and opens an opportunity to apply for patents internationally. It also gives an extended period of time to the applicants to decide on cost-intensive national or regional fittings (Grupp and Schmoch 1999).

The publication data was also used to identify important Estonian institutions in biotechnology, in order to complement the information retrieved from other sources.

In order to assess patent and publication activities more adequately, indicators reflecting the size of the various countries were taken into account and patent and publication intensities were calculated. For this purpose we used population data and data on the number of researchers in general as it is available from the OECD and Eurostat (OECD 1997, 2002). Unfortunately, data on researchers in the life sciences only or even in biotechnology are not available for international comparison. Thus, the data used can only provide a rather coarse picture related to biotechnology.

A1.2 International development of biotechnology innovation systems

The target of this working step is the analysis of the situation of biotechnology on an international level as basis for benchmarking the activities in Estonia with other countries. The biotechnology innovation systems in Austria, Finland, Germany, Ireland and the United Kingdom were analysed, using a set of quantitative performance parameters related to research and commercial activities as well as qualitative indicators to cover the framework conditions and influential factors for the national biotechnology innovation system. The selection of countries for comparison with Estonia was oriented on the size and relevance of the biotechnology sector in the different countries. An additional parameter was the matching of the profile of biotechnology activities in Estonia and the other countries. In addition, background information about the USA were gathered and taken into account for the analysis.

An additional set of activities was related to the analysis of the biotechnology innovation system in selected European benchmarking countries (Austria, Finland, Germany, Ireland, United Kingdom) and the USA. In order to collect the required information, the project team of Fraunhofer ISI used already performed studies, available statistics as well as created new data (e. g. the bibliometric and patent information). In this context reports of Ernst & Young or national institutions (e. g. statistical offices, biotechnology associations) were screened for the development and activities of biotechnology companies in the different countries. The financing of companies was analysed with the help of statistical information provided by the European Private Equity and Venture Capital Association (EVCA) as well as EU and national public funding possibilities. In addition, EU and national statistics were screened for information related to the structure of important application industries of biotechnology. Field trials with GMOs and product approvals in the pharmaceutical and biotechnology field were analysed using published data of the responsible authorities of the EU (e. g. EMEA[14], IHCP[15]). Finally, bibliometric and patent data were created for the selected countries in order to have comparable information to those of Estonia.

A1.3 Benchmarking of the Estonian biotechnology innovation system

The aim of this working step was to compare the Estonian biotechnology innovation system to that of the other countries (Austria, Finland, Germany, Ireland and the United Kingdom) in order to get hints concerning international best practices in this field. It provides information to the specific strength and weaknesses of the biotechnology location Estonia. The emphasis of the benchmarking activity will be on the framework conditions for R&D activities and commercialisation of biotechnology in the different countries.

For the international benchmarking of the Estonian biotechnology innovation system two sets of indicators were used. The first set comprises indicators providing information on the performance of the biotechnology science base. The second set is made up of indicators for commercial performance. Benchmarking of Estonia will be made against the biotechnology innovation systems of Austria, Finland, Germany, Ireland and the United Kingdom. Since these countries are quite different in their size and accordingly in their input factors to innovation, relative indicators (intensities) will be used for benchmarking. As a variable for size the population of the country will be used, as a variable for input to the innovation system the number of researchers (full time equivalent) will be applied. Possible other variables such as GDP or GERD are not available for the whole period of analysis (1990 to 2001) for all countries, so that they are less suitable as references.

The reference measures (population and number of researchers) are taken from the most recent OECD publication on science and technology indicators (OECD 2002).

The following indicators were used for benchmarking scientific performance:

- Publishing intensities in biotechnology for the two periods 1990 to 1995 and 1996 to 2001 measured as publications per million capita[16]. This indicator provides information on scientific activities as measured by publications taking account of the different country sizes.

---

[14] European Agency for the Evaluation of Medicinal Products

[15] Joint Research Center Institute for Health and Consumer Protection (located in Ispra, Italy) which is repsonsible for collecting data on field trials with GMOs in the EU.

[16] Publication data as well as patent data are gathered as described in the previous chapters.

- Growth of biotechnology publishing activities measured as growth rate of publications per million capita between the two periods mentioned above. This indicator allows conclusions on the dynamics of the development of scientific activities corrected for different country sizes.
- Biotechnology publishing intensities related to the number of researchers (publications by thousand researchers) which can be considered as a measure for the publishing activities of the research system. Since there are no comparative data available on the number of researchers in biotechnology for the countries considered, total researchers across all disciplines are used as a reference. This methodological limitation may lead to a certain distortion of the figures, if for example publishing propensities are very different between different scientific disciplines in the countries considered.
- Significance of biotechnology at the beginning of the 1990s (1991) and at the beginning of the new century (2001). Significance of biotechnology is measured as the share of biotechnology publications in all publications of each country. The measure provides information on the role of biotechnology within the research community of each country. Comparisons between the two periods allow conclusions on dynamics.
- In order to obtain a broader view on the science base which might be relevant for biotechnology, we also include some indicators on publishing activities in life sciences as a whole. As discussed in the previous chapters life sciences in total include in addition to our biotechnology categories mainly publications in the medical area and in clinical research. The following three indicators will be used: life sciences' publishing intensities measured as publications per million capita for two periods and also the growth rate between the two periods.

For benchmarking commercial performance of the different national systems the following indicators will be applied:

- The specific number of biotechnology firms in the year 2000 in each country measured as the number of firms per million capita.
- Specific venture capital invested in biotechnology during the period 1996 to 2000 which is measured as purchasing power parity per capita. Venture capital invested in biotechnology gives an indication on the appreciation of the biotechnology industry in a country by venture capital firms. Since venture capitalists usually apply a whole set of different performance indicators before placing any investment, the amount of venture capital invested in a certain industry can be considered as a combined performance indicator.
- Specific field trials of GMO (confined to plants) during the period 1996 to 2000 measured as approved notifications of field trials per million capita. This measure provides an indication on the commercial orientation of agro-food biotechnology in a country.

- Biotechnology patenting intensities for the two periods measured as patent applications per million capita. Patenting intensities yield information on the extent of application orientated research and experimental development.
- Dynamics of biotechnology patenting intensities by comparing growth rates between the two periods under consideration.
- Biotechnology patenting intensities related to researchers (patents per thousand researchers) for the period 1996 to 2001. This indicator allows conclusions on the propensity of researchers to patent their results. It can be considered as a measure for the commercial orientation of the research system. For this intensity measure the same precautions have to be kept in mind as already mentioned for the respective publication intensities: due to lacking data, only total researchers and not biotechnology researchers can be used as a reference.

For each of the described indicators the respective country values are calculated and the countries are ranked according to their indicator value.

A1.4 Recommendations for policy

During this working step the project team of Fraunhofer ISI elaborated preliminary policy recommendations as input for the formulation of the national biotechnology programme of Estonia. Recommendations for policy actions are developed in the following areas:

- Development and adjustment of the R&D capacities in the field of biotechnology in Estonia
- Shaping and management of public funding programmes for R&D activities in biotechnology
- Framework conditions for the realisation of promising R&D projects in this field
- Shaping of the framework conditions for commercial exploitation of modern biotechnology
- Creation of an innovation-friendly environment as well as the founding of new start-up companies in this field
- Improvement of co-operation activities between the different actor groups
- Improvement of private financing possibilities of biotechnology companies as well as foreign investments in this field
- Organisation of the innovation support network as well as company-related services in the biotechnology sector
- Development of the regulatory framework for commercial exploitation of biotechnology in Estonia

- Actors and framework condition for investments of international biotechnology and pharmaceutical companies in Estonia

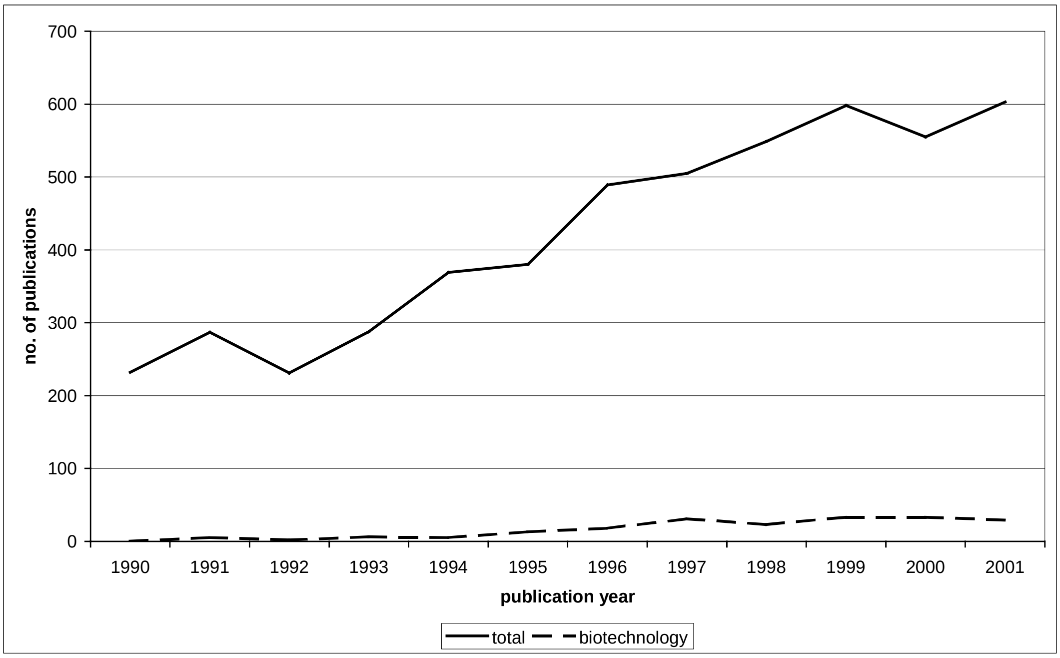
The preliminary recommendations will be presented to the Ministry of Economic Affairs and Communications and the international expert group and will serve as a starting point for intensive discussion during a workshop held on January 24th, 2003. At this workshop the representatives of the Ministry of Economic Affairs and Communications, Estonian biotechnology experts and the international expert group involved suggested some modifications of the draft final report which were included by the project team. With Estonian companies, research institutions and other actors involved in the Estonian biotechnology innovation system policy recommendations will be discussed and derived at a stakeholder meeting scheduled for February 25th, 2003 in Tallinn.

A2 Results of the bibliometric analysis

In order to describe the scientific output of Estonian researchers, bibliometric analyses were performed. Data was gathered for Estonia and the benchmarking countries. Additional data focusing on these benchmark countries will be found in those chapters dealing with the individual countries (see annex A4 - A9).

Publication output in biotechnology was increasing in all countries taken into account for the analysis as well as in total. This again confirms the specific role of biotechnology as a key technology. Compared to other countries the total number of scientific publications in biotechnology is – as it was expected – rather low in Estonia, with also low figures in the total publication output of the country (figure A2.1).

Figure A2.1 Estonian publication output – total vs. biotechnology



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

The USA and the European Union, which are the most active players in biotechnology, are producing about the same number of publications annually. As can be seen from figure A2.2 the development of their publication activities is identical since the early 1990s. Within Europe the United Kingdom and Germany are the most active countries, with Germany recently overtaking the UK (figure A2.3). A steep increase of publication activities in the second half of the 1990s can be found for both countries. Following behind are Austria and Finland. Ireland and Estonia are contributing the least number of publications – in absolute terms.

However, the picture is changing if the share of biotechnology publications of the overall publication output of one country is taken into account (figure A2.4): Finland is the country where biotechnology contributes highest to the nations publication output. Austria, the USA and meanwhile Ireland are following closely. In particular for Ireland the share of biotechnology publications was increasing in the second half of the 1990s. Germany and the UK are close together also when comparing the shares of biotechnology publications. Again Estonia is behind the other countries taken into account, and due to the low absolute numbers shares are varying stronger between the years than it can be observed for the other countries.

As we can see from figure A2.5 the Estonian position in international comparison is changing when the share of biotechnology publications is considered in relation to the output in the life sciences[17] only. Starting from well behind Estonia in 2001, reached a midfield position, at exactly the same level as the EU in total. Finland and the United Kingdom were overtaken. About 19 % of all Estonian life science publications were biotechnology related in 2001. However, it is not surprising, taken the results of the publication analysis in general, that the absolute number of Estonian publications in the life sciences is comparatively low. Figures 3.6 and 3.7 show that the USA is the most active producer of life science publications. In the life sciences the publication activities of USA exceed those of the member countries of the European Union. Within the EU the United Kingdom and Germany are again the most active countries. Due to the small country size, Estonia has a relatively low number of life science publications as well - also compared to the smaller countries that were considered for the analysis.

The situation for Estonia remains the same when publication intensities are considered. Figure A2.8 shows that all countries increased their publication activities relative to their overall population counts[18]. The highest publication intensity was determined for Finland. Already in the first period 1990-1995 Finland was at the top position and was able to extend its leading position further. More than 650 publications per million capita were published by Finnish researchers in biotechnology between 1996 and 2001. The United Kingdom comes second, being already quite significantly behind with 479 publications. The USA and Austria follow closely. Germany is still slightly above the average value of 318 publications that was calculated for the European Union in total. Estonia is considerably behind, with less than half of the publications per million capita compared to the EU value.

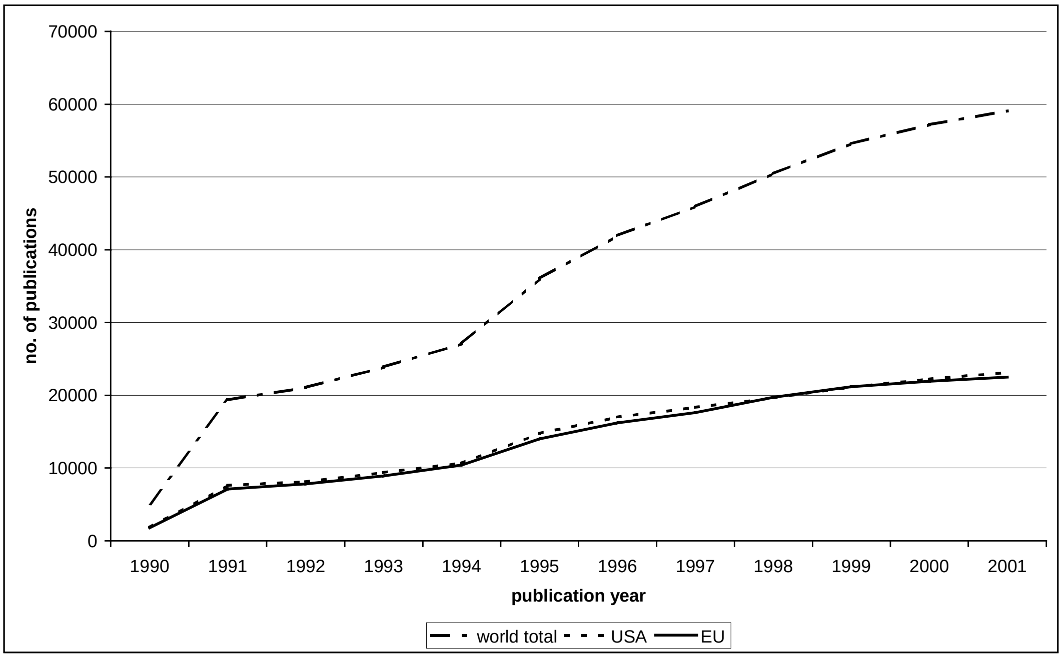
If publication intensities are calculated based on the number of researchers (figure A2.9) the situation is, apart from the fact that Estonia remains at the very

[17] The SCI as offered by the host STN can be divided into 6 data base segments. One of those is restricted to the life sciences, which was considered for the analysis.

[18] Population counts were calculated for both periods. The data used are average values. The annual data – as far as available – was added and divided by the number of years that data was available.

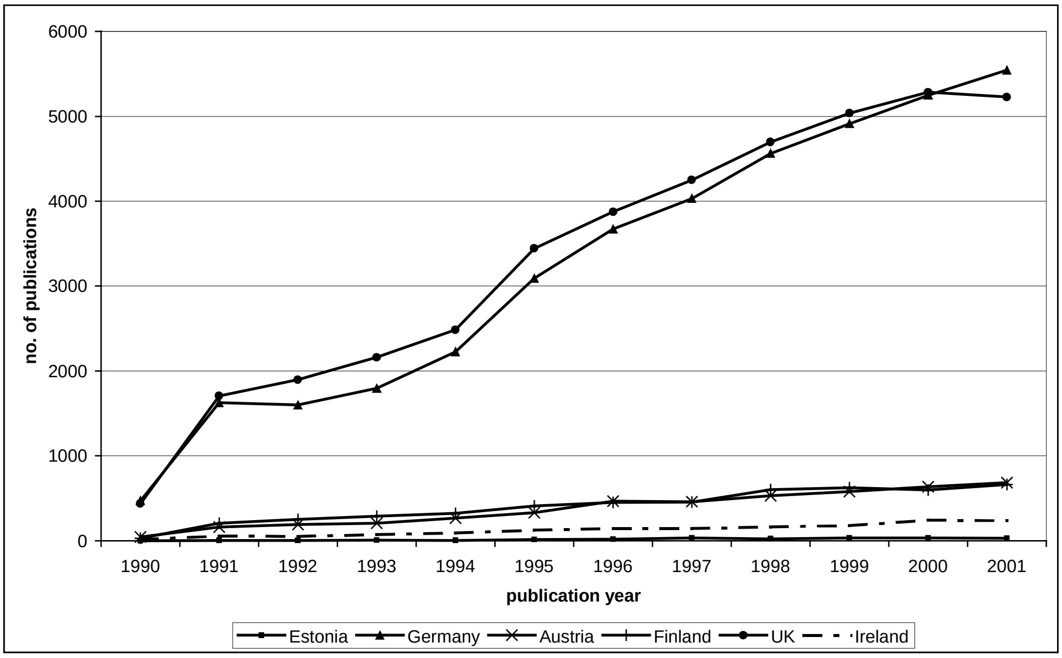
end, quite different. Finland, taken this indicator, loses its leading position and is now situated in midfield, while the United Kingdom moves to the top with 190 publications per thousand researchers. Austria follows closely with about 180 publications per thousand researchers. Ireland could improve its position and comes third. The publication intensity of Germany and the USA is lower than the value calculated for the European Union. Estonia, having about 55 publications per thousand researchers, reaches between 1996 and 2001 about the level that was calculated for the USA and Germany for the earlier period (1990 to 1995).

Figure A2.2: Number of biotechnology publications – total, USA, European Union



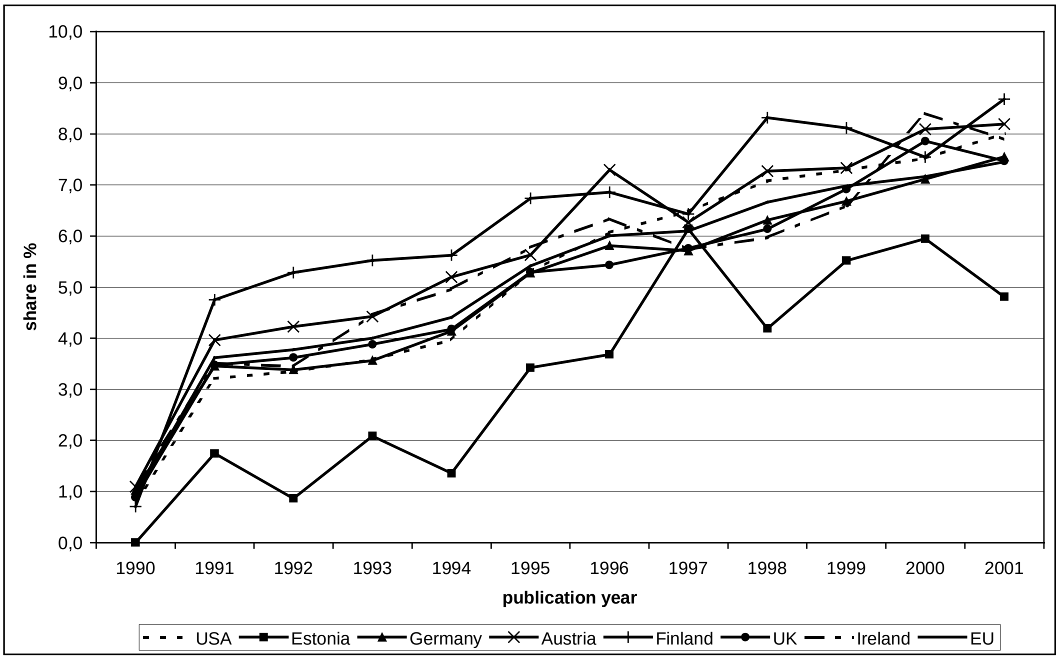
Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Figure A2.3: Number of biotechnology publications – Estonia in comparison to selected European countries



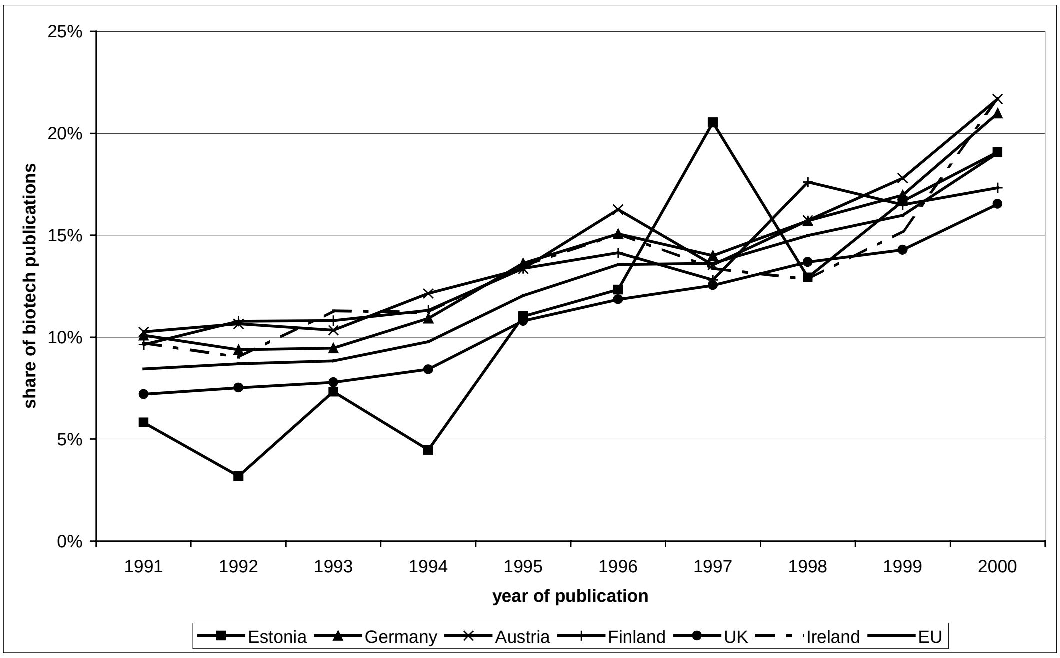
Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Figure A2.4: Share of biotechnology publications – total publication output



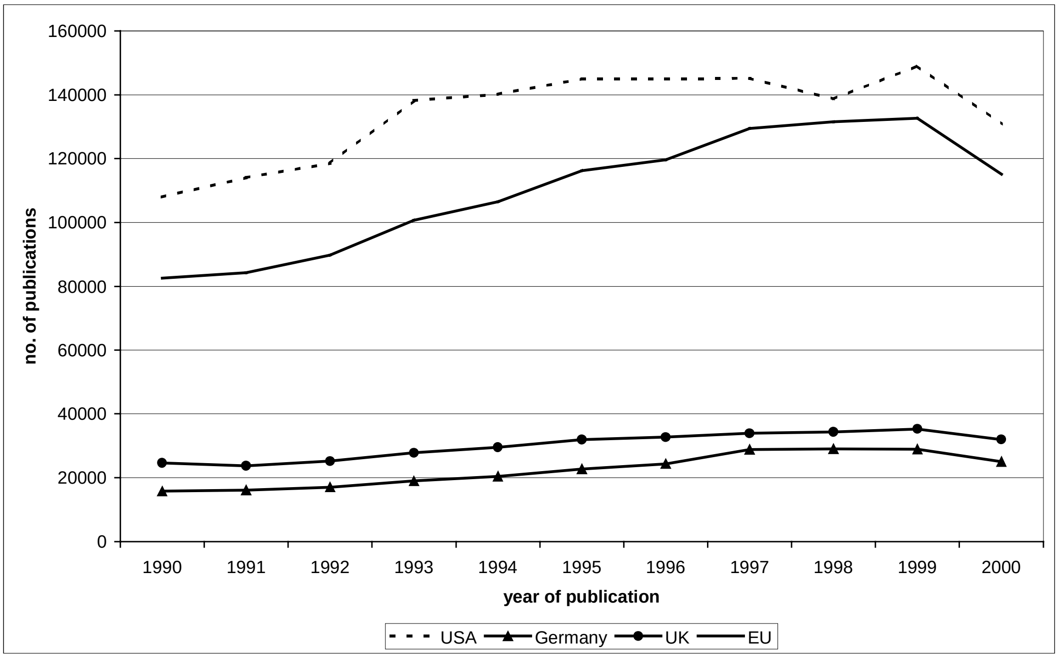
Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Figure A2.5: Share of biotechnology publications – publication output in life sciences



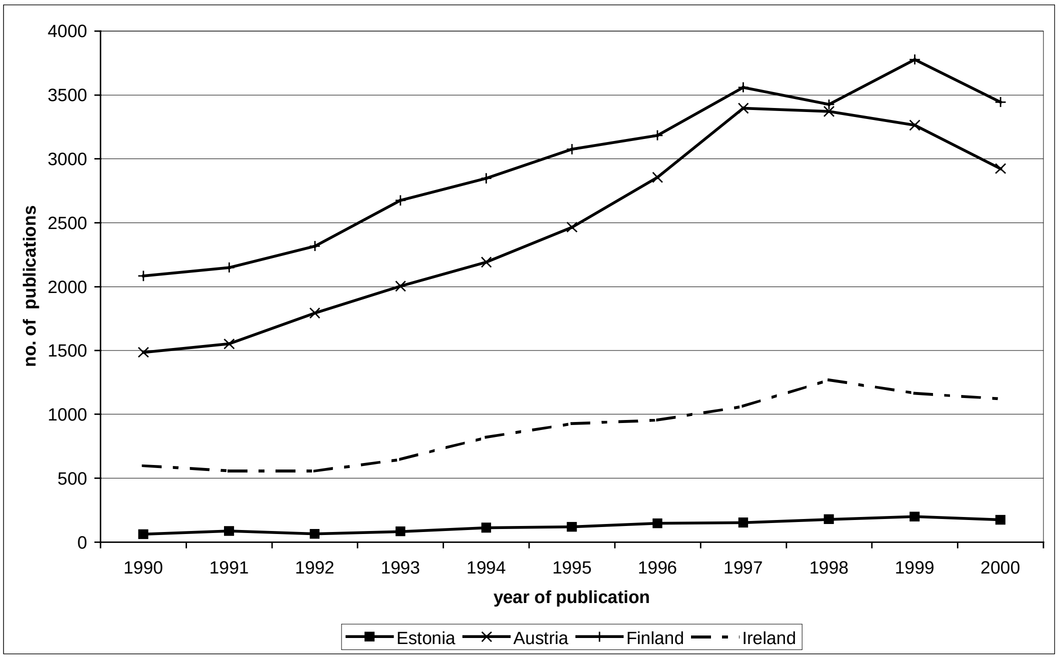
Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Figure A2.6: Number of publications in the life sciences – the top producing countries



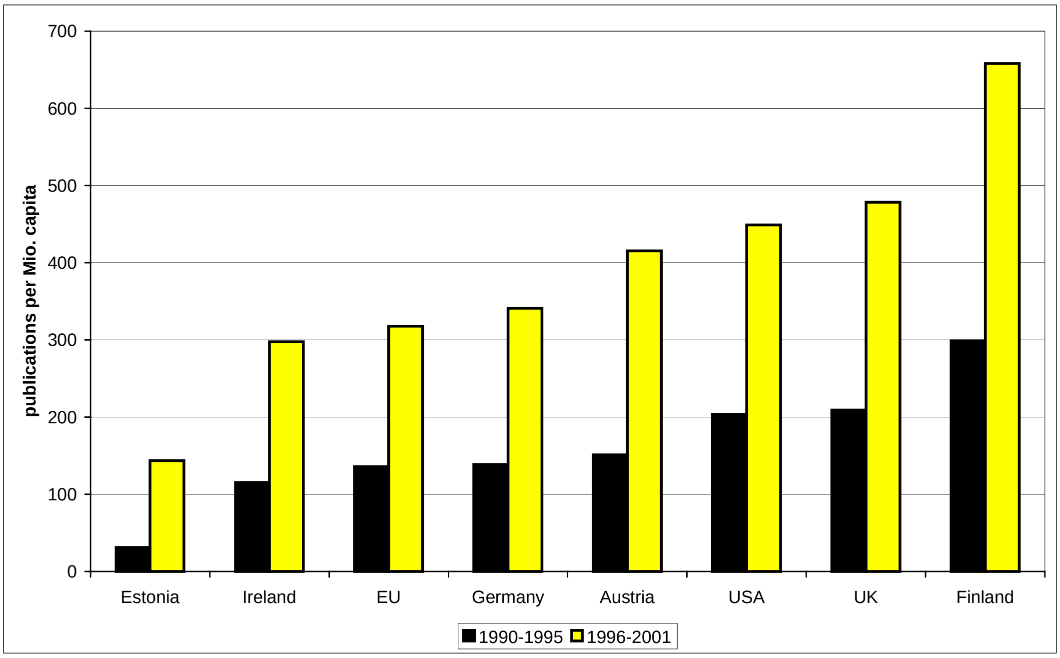
Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Figure A2.7: Number of publications in the life sciences – Estonia compared to selected European countries



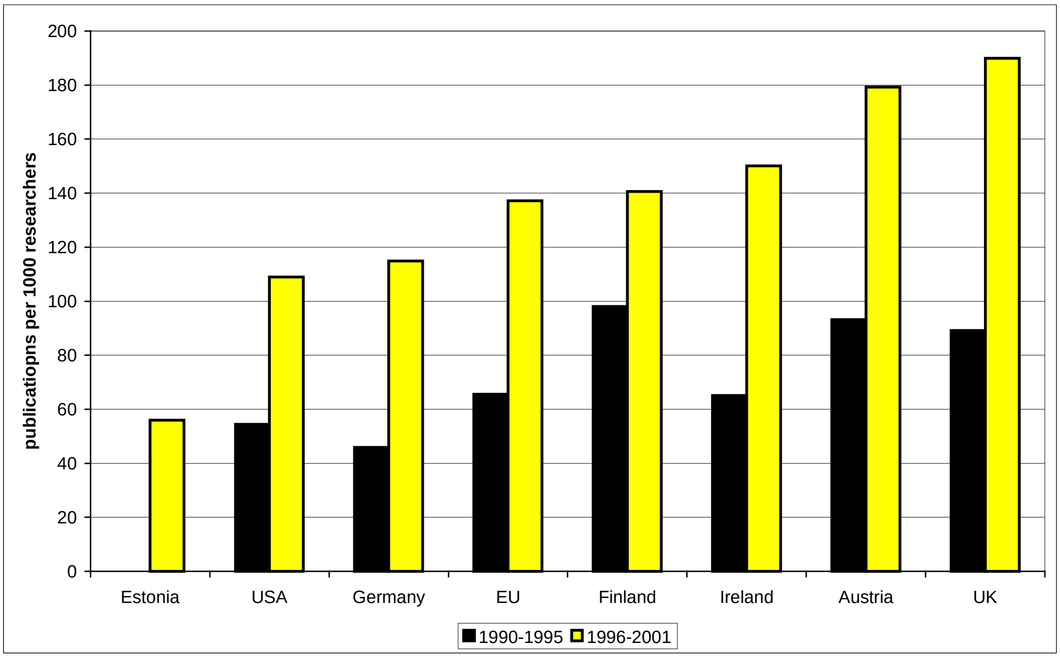
Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Figure A2.8: Scientific publications in biotechnology per million capita



Source: Fraunhofer ISI 2002, publication data: Science Citation Index via STN; population data: OECD 1997 and 2002, Eurostat 2002, Statistisches Bundesamt 2002

Figure A2.9: Scientific publications in biotechnology per thousand researchers (FTE)



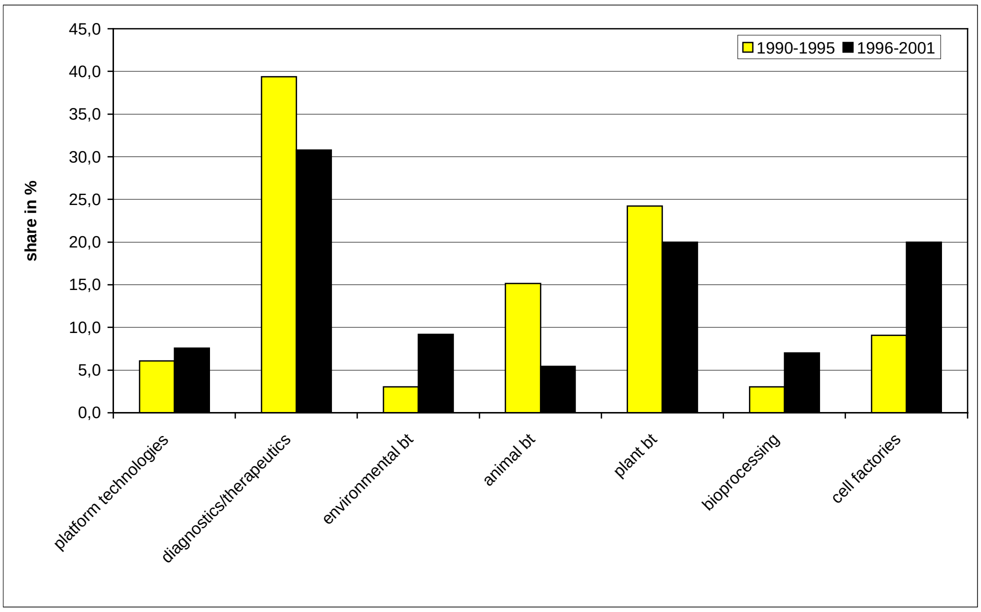
Source: Fraunhofer ISI 2002, publication data: Science Citation Index via STN; population data: OECD 1997 and 2002, Eurostat 2002

In order to analyse the focus of Estonian biotechnology, we divided the overall area into seven subareas: animal biotechnology, plant biotechnology, environmental biotechnology, diagnostics and therapeutics, bioprocessing, platform technologies and cell factories[19]. As shown in figure A2.10 there is a strong focus on biomedical research (for diagnostics and therapeutics) in Estonia. During the first period analysed (1990 to 1995) almost 40 % of all biotechnology publications were in this area. Its share was, however, decreasing to about 30 % during the second period (1996 to 2001). Also the proportion of plant biotechnology, the second most important subarea, was decreasing, from 24 % to 20 %. The same trend can be observed for animal biotechnology, which used to be the third largest subarea. Its share went down from about 15 % to 5 %. Increasing publication activities were in particular found for the subarea cell factories, which is now, during the second half of the 1990s, at the same level as plant biotechnology. Thus, this subfield increased its share from 9 % to 20 %. However, for the subarea cell factories a strong increase of publication numbers was found for all countries between 1994 and 1995, which leads to the assumption that changes of the database coverage are at least partly responsible for the observed high increase in absolute numbers. This influences, at

19 The area of cell factories covers all kinds of biotechnology research focused on the cell as producer of all sorts of products.

least partly, also relative indicator values and thus, some of the registered increase in the share of cell factories publications might be due to database effects. Environmental biotechnology is the subfield with the second largest growth during the period analysed. Platform technologies and bioprocessing showed also increasing activities, but all three areas remain on a relatively low level.

Figure A2.10: Specialisation profile of Estonian biotechnology



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

The institutions identified as contributing to the Estonian publication output in biotechnology are displayed in table A2.1. Between 1990 and 1995 the Institute for Chemical Physics and Biophysics, Tallinn, was the most active institution publishing scientific articles related to biotechnology. In the second period analysed this institute is still one of the most important players in Estonia being number two in the ranking list behind the Institute for Molecular and Cell Biology at the Tartu University (table A2.2), which significantly increased its publication output in the latter period. Other important actors are the Institute of General and Molecular Pathology at the Tartu University and the Estonian Biocentre, which is also located in Tartu. In total, the Tartu University with its various departments and institutes is most heavily engaged in biotechnological research in Estonia.

Table A2.1: Institutions active in biotechnology-related publication in Estonia between 1990 and 1995

1990-1995			
No. of publications	**Institution***		**Location**
10	INST CHEM PHYS & BIOPHYS		TALLINN
6	TARTU UNIV	INST GEN & MOLEC PATHOL	TARTU
5	TARTU UNIV	DEPT INTERNAL MED	TARTU
2	REPUBL ENDOCRINOL CTR ESTONIA		TARTU
2	TALLINN TECH UNIV	DEPT CHEM ENGN	TALLINN
2	TARTU UNIV	DEPT PEDIAT	TARTU
2	TARTU UNIV	INST PHYS CHEM	TARTU
1	INST CHEM		TALLINN
1	INST EXPTL BIOL		TALLINN
1	INST GEOL		TALLINN
1	ESTONIAN BIOCTR		TARTU
1	ESTONIAN FOREST RES INST		TARTU
1	INST EXPTL & CLIN MED		TALLINN
1	INST ZOOL & BOT		TARTU
1	REPUBL VET LAB		TALLINN
1	TALLINN TECH UNIV	DEPT FOOD CHEM & TECHNOL	TALLINN
1	TALLINN TECH UNIV	not defined	TALLINN
1	TARTU UNIV	INST MOLEC & CELL BIOL	TARTU

* The institutions partly emerge with different names in the SCI database, in particular if they have changed their name in recent years. All publications which could be identified for a specific institution are aggregated under one name.

Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Table A2.2: Institutions active in biotechnology-related publications in Estonia between 1996 and 2001

1996-2001			
No. of publications	**Institution***		**Location**
44	TARTU UNIV	INST MOL & CELL BIOL	TARTU
27	INST CHEM PHYS & BIOPHYS		TALLINN
23	ESTONIAN BIOCTR		TARTU
17	TARTU UNIV	CHILDRENS HOSP	TARTU
15	TARTU UNIV	INST GEN & MOL PA	TARTU
11	TARTU UNIV	INST PHYS CHEM	TARTU
10	ESTONIAN INST EXPT & CLIN MED		TALLINN
10	TARTU UNIV	DEPT PHARMACOL	TARTU
7	INST ZOOL & BOT		TARTU
6	TARTU UNIV	INST BOT & ECOL	TARTU
3	TARTU UNIV	not defined	TARTU
5	TARTU UNIV	DEPT INTERNAL MED	TARTU
4	TALLINN TECH UNIV	not defined	TALLINN
4	TARTU UNIV	DEPT IMMUNOL	TARTU
4	TARTU UNIV	DEPT MED	TARTU
3	ESTONIA CANC CTR		TALLINN
3	TALLINN TECH UNIV	CTR GENE TECHNOL	TALLINN
3	TALLINN TECH UNIV	INST CHEM	TALLINN
3	TARTU UNIV	INST CHEM PHYS	TARTU
3	TARTU UNIV	DEPT PATHOPHYSIOL	TARTU
3	TARTU UNIV	INST ZOOL & HYDROBIOL	TARTU
2	TALLINN CHILDRENS HOSP		TALLINN
2	ESTONIAN AGR UNIV	INST ANIM HUSB	TARTU
2	ESTONIAN AGR UNIV	INST ZOOL & BOT	TARTU
2	TALLINN TECH UNIV	DEPT BIOCHEM	TALLINN
2	TALLINN TECH UNIV	INST BASIC & APPL CHEM	TALLINN
2	TARTU UNIV	DEPT PEDIAT	TARTU
2	TARTU UNIV	DEPT PULM MED	TARTU
1	AS BIMKEMI EESTI		TALLINN
1	ASPER LTD		TARTU
1	BLOOD BANK		TALLINN
1	CENT HOSP PURU		PURU
1	CENT HOSP RAKVERE		RAKVERE
1	CHILDRENS OUTPATIENT CLIN		TALLINN

Table A2.2 continued

1996-2001			
No. of publications	**Institution***		**Location**
1	ESTONIAN ACAD SCI	INST ECOL	TALLINN
1	ESTONIAN AGR UNIV	INST ANIM SCI	TARTU
1	ESTONIAN AGR UNIV	INST EXPT BIOL	KHARKU
1	ESTONIAN AGR UNIV	INST ZOOL & BOT	RANNU
1	ESTONIAN ENVIRONM INFORMAT CTR		TALLINN
1	ESTONIAN INST ECOL		TARTU
1	ESTONIAN INST EXPT & CLIN MED		TARTU
1	ESTONIAN RES INST AGR	LAB FEEDS	SAKUHARJ UMA
1	INST ZOOL & BOT	LIMNOL STN	RANNU
1	KARKSI NUIA OUTPATIENT DEPT	VILJANDI	VILJANDI
1	MERIMETSA HOSP	STATE REFERENCE LAB AIDS DIAGNOST	TALLINN
1	NATL BOARD HLTH		TALLINN
1	TALLINN CENT HOSP		TALLINN
1	TALLINN DIAGNOST CTR		TALLINN
1	TARTU STATE HOSP	DEPT ENDOCRINOL	TARTU
1	TARTU UNIV	DEPT MICROBIOL & VIROL	TARTU
1	TARTU UNIV	DEPT OPHTHALMOL	TARTU
1	TARTU UNIV	DEPT PEDIAT SURG	TARTU
1	TARTU UNIV	DEPT PHYSIOL	TARTU
1	TARTU UNIV	DEPT PSYCHIAT	TARTU
1	TARTU UNIV	INST BIOCHEM	TARTU
1	TARTU UNIV	INST STOMATOL	TARTU
1	TARTU UNIV	LUNG HOSP	TARTU
1	TARTU UNIV	WOMENS HOSP	TARTU
1	UNIV TARTU	CTR GENE TECHNOL	TARTU
1	UNIV TARTU	DEPT PATHOANAT	TARTU
1	UNIV TARTU	HOSP ENDOCRINOL	TARTU
1	UNIV TARTU	INST ANAT	TARTU
1	TARTU UNIV	DEPT CARDIOL	TARTU
1	TARTU UNIV	DEPT CLIN PHYSIOL	TARTU

* The institutions partly emerge with different names in the SCI database, in particular if they have changed their name in recent years. All publications which could be identified for a specific institution are aggregated under one name.

Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Analysing competencies of the biotechnology research institutions all master techniques in genomics, proteomics, microbiology, cell biology, physiology, model animals, fermentation technology, downstream processing, molecular analysis and bioinformatics. There seems to be a lack of knowledge in some aspects of green biotechnology and in the field of biotechnology-related engineering. Latter may be due to the decline of engineering perspectives (esp. precision engineering) after independence from the Soviet Union when the former market for precision engineering vanished and let to unemployment and the shut down of companies.

A3 Results of the patent analysis

In order to describe the output of Estonian activities devoted towards applied research and technological development patent analyses were performed. Again we gathered data for Estonia and the benchmarking countries. Additional data focussing on those benchmark countries will be found in the respective chapters dealing with the individual countries (see annex A4 - A9).

The results of the patent analysis confirm to a large extent the information gathered form the interviews. Estonian actors are indeed not heavily engaged in patenting. This fact relates to all fields of science and technology since only 43 patents granted at the European Patent Office could be identified from Estonian institutions between 1990 and 2000. As a consequence only very few patents could be found also for biotechnology.

Compared to other countries patent intensity is very low in Estonia as can be seen from figures 3.23 and 3.24. Estonia is well behind all countries taken into account. Using overall population data[20] patent intensity was highest in the USA. Germany and the United Kingdom are following behind with quite some distance. Comparing the early nineties and the second half of the nineties those three countries increased their patent intensity significantly. Also a significant increase was found for Ireland. For Austria on the other hand we identified a rather stagnating patent intensity. Slightly decreasing was the Finnish patent intensity between the two periods analysed.

If we calculate patent intensity values based on the number of researchers[21] be find a slightly different situation. The United Kingdom moved to the top position followed by the USA. Slightly behind but close together we find Germany, Austria and Ireland. All three countries are at about the same level as it was determined for the European Union in general. Ireland increased its patent intensity most significantly between the periods considered also when measured based on the number of researchers. Decreasing was the patent intensity determined for Austria and Finland. Again, Estonia is well behind all those countries.

Due to the extremely low number of patent applications in Estonia the disaggregation into subfields of biotechnology, as it was done for the scientific publications (see annex A3) is not meaningful. Between 1990 and 1995 four and between 1996

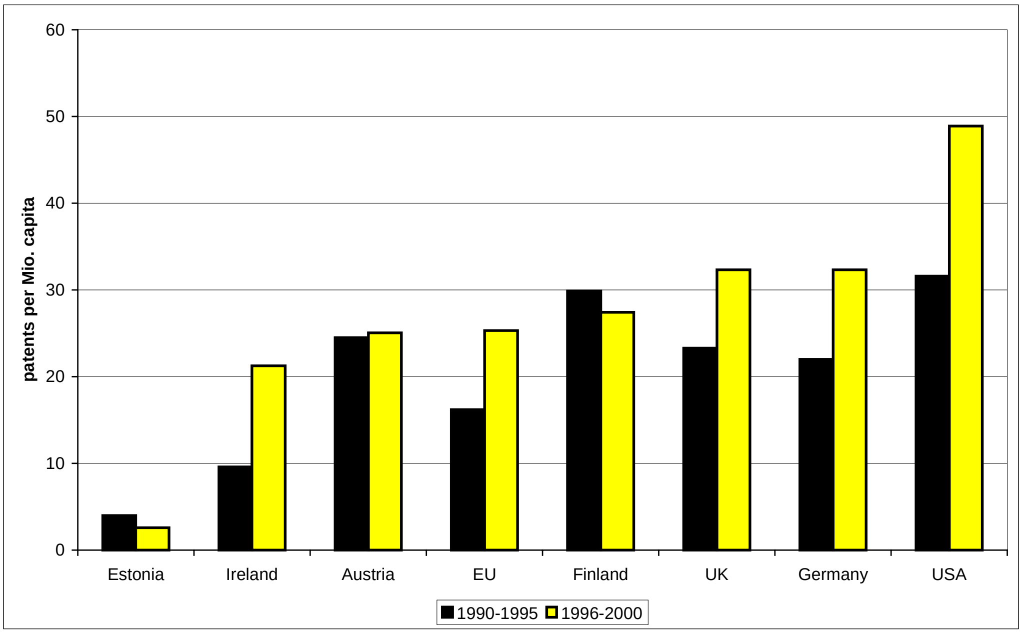
---

[20] Population counts were calculated for both periods. The data used are average values. The annual data – as far as available – was added and divided by the number of years that data was available.

[21] The number of researchers was calculated in the same way as it was done for the population counts. It refers to total number of researchers in Estonia as delimited by Eurostat (Eurostat 2002).

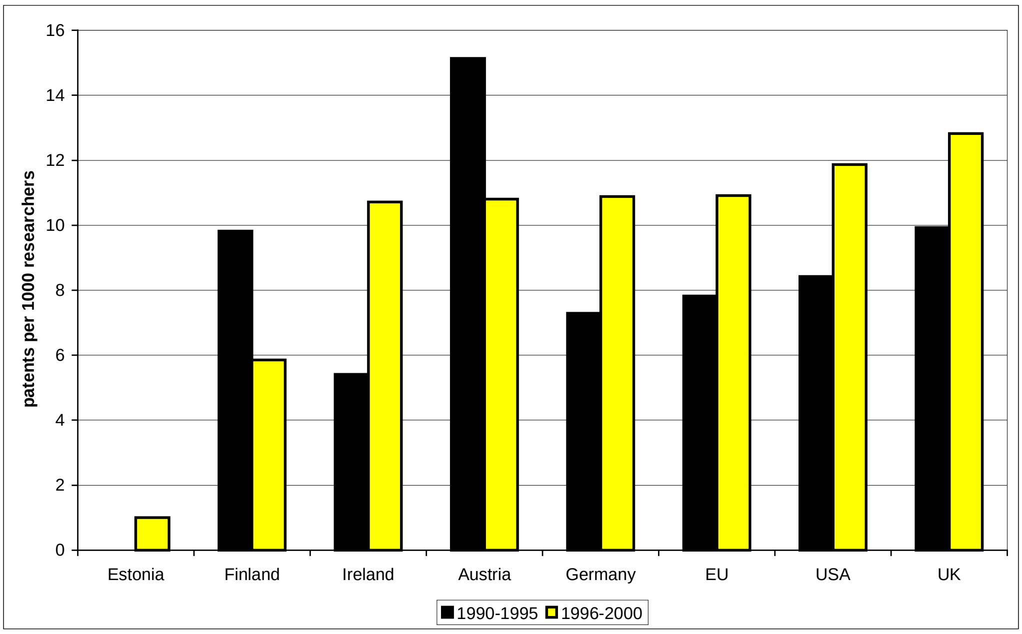
and 2000 three patent applications were filed via the international patenting procedures by Estonian actors.

Figure A3.1: Patent applications in biotechnology per million capita



Source: Fraunhofer ISI 2002, patent data: WOPatent and EPPatent via Questel; population data: OECD 1997 and 2002, Eurostat 2002, Statistisches Bundesamt 2002

Figure A3.2: Patent applications in biotechnology per thousand researchers (FTE)



Source: Fraunhofer ISI 2002, patent data: WOPatent and EPPatent via Questel; researcher data: OECD 1997 and 2002, Eurostat 2002

Although Estonian inventors were involved in those seven patent applications, which are given below, most of the patents were filed by foreign firms. For almost all patent applications international co-operative R&D activities can be assumed, which is represented by the fact that inventors from different countries are involved. One reason could be the fact that Estonian researchers spent time at those institutions that applied for the patent. The only Estonian institution that applied for a patent was the Estonian Biocentre. Estonian biotech firms, however, did not appear among the applicants so far.

1/7 EPPATENT - (C) Questel.Orbit

METHOD FOR THE PURIFICATION OF PROTEIN KINASE BY AFFINITY CHROMATOGRAPHY

IN - Loog, Mart / Rua 11-12 / 51010 Tartu (EE)
- Uri, Asko / Paeva St. 23-2 / 50103 Tartu (EE)
- Jarv, Jaak / Wiiralti St.m 31-4 / 51010 Tartu (EE)
- Ek, Pia / Nyhagen / 74030 Bjorklinge (SE)

PA - Loog, Mart / Rua 11-12 / 51010 Tartu (EE) - Uri, Asko / Paeva St. 23-2 / 50103 Tartu (EE) - Jarv, Jaak / Wiiralti St.m 31-4 / 51010 Tartu (EE) - Ek, Pia / Nyhagen / 74030 Bjorklinge (SE)

2/7 EPPATENT - (C) Questel.Orbit

METHODS AND TEST KITS FOR EVALUATING THE PRESENCE AND SEVERITY OF RESPIRATORY TRACT INFLAMMATION

IN - MAISI, Paivi / Maisinkuja 41 / FIN-01940 Palojoki (FI)
- SEPPER, Ruth / Eha 22, Kelvingi / 74001 Viimsi (EE)
- PRIKK, Kaiu / Peetrikatu 86/1 / 2400 Tarto (EE)
- RAULO, Saara / Maurinkatu 16 A 10 / FIN-00170 Helsinki (FI)
- TIKANOJA, Sari / Vainamoisenkatu 29 B 24 / FIN-00100 Helsinki (FI)
- SORSA, Timo / Lounaisvayla 17 / FIN-00200 Helsinki (FI)

PA - OY MEDIX BIOCHEMICA AB / Asematie 13 / 02700 Kauniainen (FI)

3/7 EPPATENT - (C) Questel.Orbit

CONJUGATES OF TRANSPORTER PEPTIDES AND NUCLEIC ACID ANALOGS, AND THEIR USE

IN
- LANGEL, Ulo / Trollesundvagen 21 / S-124 32 Bandhagen (SE) (Updated 2000-37)
- BARTFAI, Tamas / 2480 Rue Denise / La Jolla, CA 92037 (US) (Updated 2000-37)
- POOGA, Margus / Pikk 98-27 / EE2400 Tartu (EE) (Updated 2000-37)
- VALKNA, Andres / Aardla 69 / EE2400 Tartu (EE) (Updated 2000-37)
- SAAR, Kulliki / Olror,Salgstigen 37 / S-181 62 Lidingo (SE) (Updated 2000-37)
- HALLBRINK, Mattias / Professorsslingen 23 / S-104 05 Stockholm (SE) (Updated 2000-37)

PA
- THE PERKIN-ELMER CORPORATION / 850 Lincoln Centre Drive / Foster City, California 94404 (US)
- PERSEPTIVE BIOSYSTEMS, INC. / 500 Old Connecticut Path / Framing ham, MA 01710 (US) (Updated 2001-24)

4/7 EPPATENT - (C) Questel.Orbit

PARALLEL PRIMER EXTENSION APPROACH TO NUCLEIC ACID SEQUENCE ANALYSIS

IN
- Caskey, Thomas C. / 6402 Belmont / Houston, TX 77005 (US)
- Shumaker, John / 719 Pizer / Houston, TX 77009 (US)
- Metspalu, Andres / 4-33 Kaunase Street / Tartu 2400 (EE)

PA
- Pharmacia Biotech AB / 751 82 Uppsala (SE)
- BAYLOR COLLEGE OF MEDICINE / One Baylor Plaza / Houston, TX 77030 (US)

5/7 EPPATENT - (C) Questel.Orbit

EPISOMAL VECTOR AND USES THEREOF

IN - USTAV, Mart / Jaama Street 58A / EE2400 Tartu (EE)

PA - Estonian Biocentre / 23 Riia Street / 2400 Tartu (EE)

6/7 EPPATENT - (C) Questel.Orbit

PARALLEL PRIMER EXTENSION APPROACH TO NUCLEIC ACID SEQUENCE ANALYSIS

IN - CASKEY, C., Thomas / 6402 Belmont / Houston, TX 77005 (US)
- SHUMAKER, John / 719 Pizer / Houston, TX 77009 (US)
- METSPALU, Andres / 4-33 Kaunase Street / Tartu 2400 (EE)

PA - Pharmacia Biotech AB / / S-751 82 Uppsala (SE) - BAYLOR COLLEGE OF MEDICINE / One Baylor Plaza / Houston, TX 77030 (US)

7/7 EPPATENT - (C) Questel.Orbit

TRANSGENIC PLANTS DISPLAYING MULTIPLE VIRUS RESISTANCE AND A PROCESS FOR THEIR PRODUCTION.

IN - Truve, Erkki / Madala 5-47 / 10311 Tallinn (EE) (Updated 2000-21)
- Kelve, Merike / Kaupmehe 15-8 / 10114 Tallinn (EE) (Updated 2000-21)
- Teeri, Teemu / Porttitie 17 B / 02180 Espoo (FI) (Updated 2000-21)
- Saarma, Mart / Kalosaaren puistotie 38 A 4 / 00570 Helsinki (FI) (Updated 2000-21)

PA - KEMIRA BIO HOLDING B.V. / P.O. Box 8105 / NL-3196 ZG Vondelingenplaat Rt (NL) - Truve, Erkki / Madala 5-47 / 10311 Tallinn (EE) (Updated 2000-21)
- Kelve, Merike / Kaupmehe 15-8 / 10114 Tallinn (EE) (Updated 2000-21)
- Teeri, Teemu / Porttitie 17 B / 02180 Espoo (FI) (Updated 2000-21)
- Saarma, Mart / Kalosaaren puistotie 38 A 4 / 00570 Helsinki (FI) (Updated 2000-21)

A4 Biotechnology innovation system in Austria

A4.1 Introduction

The Austrian population amounts to 8.1 million people in the year 2000. The main sector of the economy is industry followed by tourism. Although Austria ranks in terms of GDP per capita and productivity among the leading industrialised nations, the biotechnology scene developed very late compared to other European countries. One reason is the rather strong fragmentation of the research and technology policy in Austria. Several federal ministries and other funding organisations have issued their own funding activities directed towards different technologies. Top-down funding activities in the frame of specific technology programmes are rather new elements having emerged in the last decade.

According to figures of the OECD (2002) the gross domestic expenditure on R&D (GERD) amounted up to 3,942 million PPP in 2000. Indicators such as the ratio of GERD to GDP are still below European or OECD averages. The Austrian GERD share in GDP came to 1.80 % compared to 1.88 % in the EU and 2.24 % in the OECD. However, the GERD share in the GDP increased since 1996. GERD per capita population was 486.1 PPP in the year 2000 which is slightly more than the European average of 457.7 PPP in the same year. Since 1996 per capita GERD increased continuously in Austria. 41 % of GERD was financed by industry in the year 2000. This shows that the industry contribution to R&D financing in Austria is rather low in the EU (55.5 %) and also the OECD (62.9 %) context. The industry contribution to GERD decreased slightly from 44.2 % in 1996 to 40.1 % in the year 2001. The total number of Austrian researchers was 18,715 (full time equivalent (FTE)) in 1998. This corresponds to a ratio of 4.7 % per thousand total employment which is clearly below the European value of 5.4 % and the OECD ratio of 6.4 % in the same year.

The following chapters will characterise the Austrian biotechnology innovation system along different dimensions. The first chapter will describe the policy framework supporting biotechnology in Austria. The second chapter gives its attention to the performance of the Austrian biotechnology innovation system and the third chapter will summarise how different policy instruments contributed to shaping the present situation of the Austrian biotechnology innovation systems.

A4.2 Policy framework

The Austrian funding system of the 1990s is characterised by a rather fragmented situation in which different public institutions and ministries have issued their own funding activities directed towards different technologies. The main policy instrument is project funding, which again is mainly organised via a bottom-up approach. The two key players between 1994 and 1999 in the Austrian funding scene were the Fonds zur Förderung der Wissenschaftlichen Forschung FWF (Austrian Science Fund for the advancement of basic research) and the Forschungsförderungsfonds für die gewerbliche Wirtschaft FFF (Industrial Research Promotion Fund). In the beginning of 2000 a re-organisation of the Austrian innovation policy arena took place. Key players are now the Ministry of Transport, Infrastructure and Technology, the Ministry of Education, Science and Culture and the Ministry of Economy and Labour. However, the ministries still distribute their financial sources to the FFF and the FWF. Additionally there exist several funding activities at a regional level, and this is especially observable in the area around Vienna. Since at least two large pharmaceutical companies are active in biotechnology research at a substantial level, financial sources for biotechnology research can be provided at a private level as well. Another general feature of the Austrian system is that funding via specific programmes is a rather new instrument, having only emerged during the last 15 years. The funding procedure is mainly realised via open call systems.

A4.2.1 Creating and sustaining a biotechnology knowledge base

Programmes or particular initiatives aiming at supporting the knowledge base in biotechnology were not very common in Austria in the 1990s. They just gained significance during the last two to three years. With respect to policy instruments for strengthening co-operation between public research institutions and across disciplines, different initiatives (e. g. by the FWF) were already undertaken at an early stage. While in 1994 there existed no intentional policies to support applied research at universities and other public research institutions, the situation changed until 2001. Encouraging industry-oriented research became much more important.

Three programmes supporting the knowledge base were identified. The so-called *Impulse Programme Biotechnology (IPB)* was an effort to improve the fragmented funding activities. The aim was to achieve a stronger co-ordination between the different parties involved. Another general aim of the IPB was to support patenting and to better exploit research results at public research institutions. At an inter-university level the *K+ programme* is worth to mention. It aims to promote clustering and co-operation among public sector research organisations (PSRO) by supporting the establishment of competence centres. The initiative is generic, however, one of twelve competence centres is especially focusing on biomolecular therapeutics. The most popular biotechnology-related programme in Austria is the national Human Genome Project called *GEN-AU*. The programme is financed by the Austrian government and is intended to last for about ten years. The Ministry of Education, Science and Culture is organising the programme. The first phase already started and until 2005 32 million € are provided for five linked projects with a maximum of five sub-projects (Kronau 2002). The support is dedicated to research co-operations at the university and the company level.

A4.2.2 Commercialising biotechnology

As in the case of support for the knowledge base, in this category no biotechnology-specific programmes or initiatives were observable until the late 1990s either. This situation changed considerably in 1997. Different programmes were launched by the Innovation Agency Austria, by the Zentrum für Forschungsförderung (Centre of Funding Support), the Büro für Internationale Forschungs- und Technologie-kooperation (BIT) (Office for International Research and Technology Co-operation), the Centre for Molecular Pathology, or third party institutions. Especially High Performance Start Ups are already making intense use of these new commercialisation programmes.

The K+ Centres of Competence programme can be considered as an improvement with respect to policies that support the commercialisation of biotechnology. Additionally, the Impulse Programme Biotechnology (IPB) is mainly dedicated to encourage the commercialisation of scientific results from public research institutions. In order to achieve this general aim the following specific objectives have been set:

- Support of the creation of new biotech firms
- Advice for biotech researchers in patenting and exploitation of research results
- Opening financing instruments for biotechnology - Business Angels Network
- Promoting co-operation between science and industry
- Provide infrastructure and space for biotech start-ups
- Support the exploitation and commercialisation of patents
- In general, create an innovation-friendly environment
- Contribute to public information about biotechnology

With respect to instruments that support the commercialisation of technologies, including the mobility of researchers, the activities of the Industrial Research Promotion Fund (FFF) are most worthy to mention. Its main objective is to support innovation projects in the Austrian industry in the form of allocating grants for industrial research. The main target group are small and medium-sized companies which receive about two thirds of the FFF funds. During the last eight years different measures were added to the activities of the Industrial Research Fund. Firstly, in the "Relay Programme" companies are involved in research as observers right from the basic research stage. If a particular development approaches the marketing stage, the project is taken over by a company. Secondly, "Post-Docs for Industry" is a programme managed by the FWF aiming at facilitating know-how transfer from universities to industry. This occurs mainly via the support of post-docs in the industry. A third new measure is the "Young Researcher Programme". The aim of this programme is to involve young researchers in joint projects with companies. The last initiative is the "A+B programme", managed by the Technologie Impuls Gesellschaft TIG (Technology Impulse Association). The abbreviation A+B stands for Academia Plus Business and tries to stimulate the formation of university spin-off companies. In addition, the programme supports the establishment of science parks and incubators.

In general, there is currently an increasing focus on the support of new technology-based companies in Austria. In addition to the A+B programme the Innovation Agency has specifically designed three programmes for that purpose: The "Seed Financing Programme", the "Technology Marketing Austria Programme" and the "Young Entrepreneurs Programme".

Poor technology transfer in Austria may be related to the lack of any specific research programmes targeted at biotechnology or the lack of any technology transfer mechanisms until 1998.

A4.2.3 Creating a supportive framework for biotechnology

Regulations general

Since its membership in the European Union Austria had to adjust regulatory matters to an international level as well. In order to implement the European biotechnology legislation from 1990, Austria issued a specific gene technology act in 1994. In comparison to other member countries the Austrian law is considered to be more restrictive. In 1998 an amendment to the gene technology act was passed concerning among others civil liability, multi-party procedures in the case of the release of GMO, control and restoration of the environment in case of any destruction, safety documentation , and product registration. Presently there is a discussion on introducing an additional environmental impact assessment. Additionally, legislation governing pharmaceutical are very relevant for biotechnological activities in Austria.

Intellectual property rights

In 1998 the TECMA (Technology Marketing Austria) was founded by the Ministry of Economic Affairs and Communication as an organisation with the task to exploit patents. It supports the commercialisation of research results from Austrian universities, companies and private individuals by licensing and selling inventions and know-how. The major advantage for the inventors is that TECMA evaluates the invention under economic and technological aspects, looks for the appropriate license taker and pre-finances the patent application. In addition to this initiative, the already mentioned Impulse Programme Biotechnology (IPB) also intends to stimulate patenting activities among researchers.

Financing

Only few activities in this category could be detected in the time period under consideration. The availability of private venture capital for biotechnology is rather limited in Austria. However, the FWF launched a venture capital-specific programme which is in general supporting high technology companies in Austria. Furthermore, the Austrian Innovation Agency launched the "Seed-Financing-Programme", which aims to support the growth of small companies via a specifically tailored financing programme. Additionally institutional investors are financing business activities of small companies. This happens mainly at a regional level.

Socio-economic issues

Despite increasing public awareness of controversial issues concerning biotechnology, no particular policy initiatives aiming at supporting public discourses and other measures seem to be taken in Austria. The Austrian Gene Technology Law is probably the most important issue in this context and the Federal Chancellery has the main responsibility for its implementation. The law requires that scientific studies on bio-safety need to be performed. Therefore, the Federal Chancellery is supporting some research projects dealing mainly with safety issues. In addition to these funding activities, the Federal Ministry of Economic Affairs and Communication supports some projects which deal with food labelling and food safety. Since the end of the 1990s the Impulse Programme Biotechnology (IPB) dedicates its attention to issues with a socio-economic and ethical dimension as well.

Public acceptance

Non-governmental organisations are frequently involved in the socio-economic debate. These include representatives of religious groups, representatives from industry associations, greenpeace, environmental groups, such as global 2000. Since Austria is nowadays not very active in green biotechnology, the discussion about this issue is very calm.

Human capital

The recruitment of new staff at the graduate and postgraduate level is no problem at public research organisations. There are enough students available who have the relevant skills in natural sciences. However, the recruitment of post-docs is sometimes a problem, since competition from the United States is very high. Jobs are better paid there, and the working conditions are assessed as more attractive compared to Europe. The other problem is the recruitment of technicians who are supporting researchers with their technical skills. Although there exists a five-year education programme in Austria, the training system for these kinds of jobs is criticised and improvements are called for.

Recruitment of staff at the industry level is another controversial issue. Opinions diverge substantially regarding the current job situation in Austria. Some firms have no problems at all to recruit the necessary staff, others have serious problems. The availability of chemistry students and the recruitment of technicians seem to be the most important bottlenecks. Another problem exists mainly at small companies, because employees sometimes prefer working at larger companies for job security reasons. Many researchers are afraid of being too much dependent on "unstable" and small firms. Larger companies are less influenced by short-term market fluctuations that could imply substantial consequences for the employees.

A4.3 Performance of the Austrian biotechnology innovation system

A4.3.1 Performance related to scientific activities

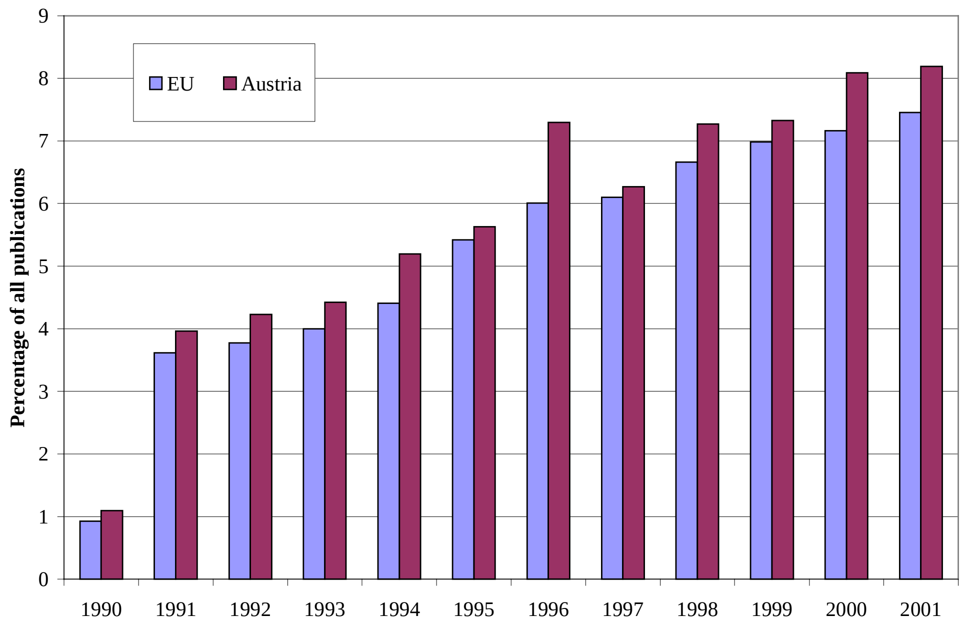
In the last years the absolute number of publications in the field of biotechnology increased. Between 1990 and 1995 1,195 biotechnological articles were published by Austrian actors. This number went up to 3,355 articles in the period between 1996 and 2001. A very significant increase of publication output in biotechnology is also obvious in the relation of publications to the number of inhabitants of the country. In the first period (1990 to 1995) 151 publications per million capita were made in Austria. In the second period (1996 to 2001) the number of publications per million capita increased intensively to 415. Compared to the European average (136 publications per million capita in the first period and 318 publications per million capita in the second period), the performance of the Austrian biotechnology system exceeds the average. The publication output related to the number of researchers[22] is an indicator for measuring the efficiency of the research system. In

[22] Since official data on the number of researcher in biotechnology are not available, we use the OECD figures for all researchers in the country.

the first period publication intensity related to the number of researchers amounted to 93 per thousand researchers, which was above the European average of 65. In the second period publication intensity increased substantially to 179 publications per thousand researchers, compared to an EU level of 137. In summary, publication indicators adjust the Austrian biotechnology innovation system above the European average, indicating a good efficiency of the Austrian system with respect to publication output.

Another indicator to assess the significance of biotechnology in the Austrian research system is the share of biotechnology publications of all Austrian publications. This indicator increased approximately linearly from 1990 to 2001. In 1990 only 1 % of all publications dealt with biotechnology. In 2001 more than 8 % of all were biotechnological publications. In this context it is noticeable that the percentage of biotechnology publications in Austria go beyond the European average in each year (figure A4.1).

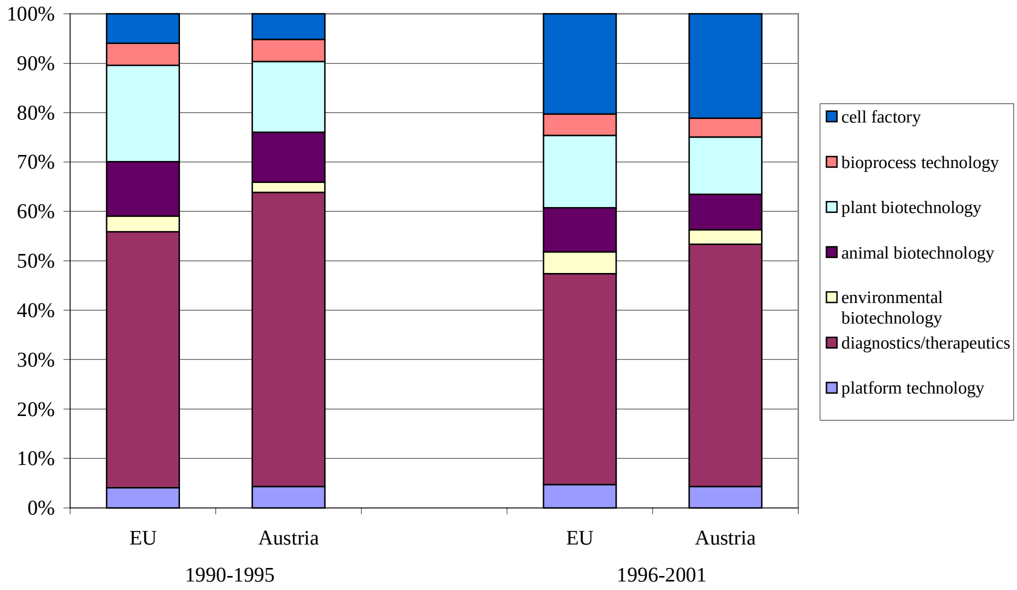
Figure A4.1: Share of publications in the field of biotechnology of all publications in Austria



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

The biotechnological profile on basis of the biotechnological publications, which is given in figure A4.2, shows the field of diagnostics and therapeutics as the most important research area in Austria. Between 1990 and 1995 nearly 60 % of all biotechnological publications came from this field. Also in the period from 1996 to 2001 diagnostics and therapeutics were with 49 % the most important biotechnological research area. The percentage of diagnostics and therapeutics in Austria were nearly 7 % higher than in the EU in both periods. Other important research areas in Austria (but underrepresented compared with the EU) are plant and animal biotechnology.

Figure A4.2: Share of different biotechnological fields in biotechnology in Austria and the EU



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

A4.3.2 Performance related to commercialisation

Biotechnology firms

In Austria the number of biotech firms is small. In 2000 59 firms were active in the biotechnological sector (Ernst & Young). Because there are no standardised data for former years, it is not possible to reflect the general development of Austrian biotech firms in the last decade. There exists only one biotech cluster in Austria – this is the area of Vienna. Austria is a country in which the number of employees concentrate in firms with over 100 employees. The median creation date of the firms was 1974. This suggests that exploitation of biotechnology is mainly by diversification, not the creation of new firms. Most of the firms are involved in pharmaceutical application. More than 90 % of the companies are active in this field (Boston Consulting Group 2001).

Venture capital invested in biotechnology

There is low availability of venture capital in Austria. Two venture capital firms are active in biotechnology but only a tiny proportion of available funds has been allocated to this sector.

Table A4.1 shows the amount of venture capital that has been invested in Austrian biotechnology in the two investigated periods 1990 to 1995 and 1996 to 2000. In the latter period around 2.5 million € venture capital has been invested in biotechnology companies. In absolute figures the amount has increased nearly six times. In relation to the biotechnology venture capital in the whole EU a slight increase can be found, too.

Table A4.1: Venture capital invested in Austrian biotechnology

Year	**absolute value**		**% of venture capital invested in EU**
	in 1,000 €	in 1,000 PPP[23]	
1990 to 1995	436.90	402.076	0.09
1996 to 2000	2534.92	2389.006	0.13

Source: EVCA

As table A4.2 indicates, the amount of biotechnology venture capital increased not only in absolute figures, but also relative to the mean population nearly sixfold in Austria but has not yet reached the EU level.

Table A4.2: Indices of venture capital invested in Austria

	Austria		**EU**	
Year	**absolute amount**	**amount relative to mean population**	**absolute amount**	**amount relative to mean population**
	in 1,000 PPP	in PPP per inhabitant	in 1,000 PPP	in PPP per inhabitant
1990 to 1995	402.076	0.051	438919.599	1.191
1996 to 2000	2389.006	0.295	1783683.684	4.760

Source: EVCA

23 PPP: purchase power parity

Initial public offerings

There was only one initial public offering (IPO) of a biotechnology company in Austria between 1995 and 2000: Sanchochemia Pharmazeutika went public in 1999[24].

Drugs approved

According to data from EMEA no bio-medicines originating from Austrian companies were approved by EMEA between 1995 and 2001.

Field trials of GMO plants

Three field trials of GM plants were notified to the EU, all in 1996. One field trial was notified for maize and two for potato (IHCP 2002). The Austrian notifications were carried out by large firms (2) and one SME and account for 0.2 % of all field trials in the EU.

Patent applications

Austrian actors applied for 194 patents for biotechnological inventions between 1990 and 1995 and for 202 patents between 1996 and 2000[25] at the European Patent Office. Most of the patents came from the subfields of diagnostics/therapeutics, platform technologies and cell factory. In the last years the number of patents increased especially in the subfield of platform technologies whereas the patent number decreased in the subfield of cell factory.

Related to population the patenting intensity increased very slightly from 24.5 biotechnology patents per million inhabitants in the first period to 25 patents per million inhabitants in the period between 1996 and 2001. Only the first value is above the European average of 16.2. As a result of the significant increase of the number of European biotechnology patents per million inhabitants to 25.3 the Austrian value in the second period was only European average. Patenting intensities related to researchers decrease from 15.1 biotechnology patent applications per thousand researchers in the first period to 10.8 patent applications per thousand researchers in the second period. Only the first value is above the European average of 7.8 for the first period. The Austrian value for the second period is again very close to the European average of 10.9 patent applications per thousand researchers.

---

24 Sources: E&Y Annual European Life Sciences Reports, websites by Nasdaq, Neuer Markt, London Stock Exchange, Euronext

25 The patent numbers for the year 2000 are estimated.

The share of biotechnology patents of all Austrian patents was 4.5 % in the first period of investigation and decreased to 4 % in the second period. This drop and also the fall back behind the EU values in the 1996 to 2000 period indicate a decreasing relative relevance of biotechnology patent applications in Austria.

A4.4 Conclusions

Compared to other European countries biotechnology in Austria is still in an early phase of development. The performance analysis indicates that Austria so far could not build up a broad internationally oriented science base in biotechnology, activities are concentrated on few centres. Commercialisation of biotechnology also lacks behind other European countries. Concerning the biotechnology-relevant policy regime of Austria during the 1990s it could be concluded:

- The fragmented policy approach with only weakly connected different instruments and no specific focus on certain technological areas such as biotechnology was not very successful in the case of biotechnology.
- However, some Austrian groups could benefit from this policy approach. These groups were not only able to take advantage of the bottom-up open call system, but also succeeded in acquiring research support from the industry. We presume that the non-specific open call system is rather effective in supporting a few leading groups because these are not only familiar with the system but also have the necessary knowledge and expertise, which further sustained through industry collaborations, for preparing grant applications. On the other hand 'newcomers' might have more difficulties with such a system.

Since the late 1990s new biotechnology-specific programmes have been launched aiming at supporting the expansion of the knowledge base, commercialisation and co-operation. Due to novelty of these programmes, it is difficult to measure already any effect using science and commercialisation indicators. But it is possible to give some general conclusions:

- Concepts differentiating between basic and applied research are not adequate for strongly science-based technologies such as biotechnology.
- Specific biotechnology programmes need careful consideration of the specific needs of target groups calling for an early involvement of stakeholders during programme design.
- Programmes and in particular programme implementation need to be flexible in order to allow adjustments to the research process.

Concerning the regulatory environment for biotechnology in Austria, lacking European harmonisation of several different regulations (e. g. IPR, exchange of materials, property situation of databank information) constitute major restraints.

A5 Biotechnology innovation system in Finland

A5.1 Introduction

Finland has a population of 5.2 million people and a gross domestic product (GDP) of 134,160 million PPP in 2001. Strong sectors are wood production and processing, the metal and engineering sector and a rapidly expanding electronics industry. Finland pursues a knowledge-based growth strategy. In 1996 the Finnish government made a decision to further substantially increase investments in R&D. The largest part of the public funding was to be channelled from the privatisation of state-owned companies.

According to figures of the OECD (2002) the gross domestic expenditure on R&D (GERD) amounted up to 4,391.6 million PPP in 2000. This corresponds to a ratio of 3.37 % GDP which is clear above the EU average (1.88 %) and the OECD average (2.24 %). The Finnish GERD share in the GDP increased since 1996. GERD per capita population was 848,5 PPP in the year 2000 which is much more than the European average of 457.7 PPP in the same year. Since 1996 per capita GERD increased rapidly in Finland. There is a very strong contribution to R&D financing by the Finnish industry. 70.2 % of GERD was financed by industry in the year 2000. This share exceeds clear the corresponding shares for the European Union (55.5 %) and for the OECD (62.9 %). The industry contribution to GERD increased since 1996. The total number of Finnish researchers was 25,398 (full time equivalent (FTE)) in 1999. This corresponds to a ratio of 11.3 % per thousand total employment which is more than twice the European value of 5.6 % and clearly above the OECD ratio of 6.6 % in the same year. In sum, these indicators show that in terms of input to R&D Finland ranks on the top of the European countries.

The following chapters will characterise the Finnish innovation system in the field of biotechnology along different dimensions. The three chapters will describe the policy framework supporting biotechnology, the performance of the Finnish biotechnology innovation system and will make some conclusions how different policy instruments contributed to shaping the present situation of the Finland biotechnology innovation systems.

A5.2 Policy framework

The first sign of governmental concern for the development and commercialisation of biotechnology is the establishment of the 'National Programme for the Development of Biotechnology and Molecular Biology' in 1988. Since then, four Ministries share the responsibility of promoting biotechnology in Finland: The Ministry of Education, the Ministry of Trade and Industry, the Ministry of Agriculture and Forestry and the Ministry of Health and Social Affairs. However, the implementation of the different policy instruments is carried out by 3 other institutions: the Technology Development Centre (TEKES), The Academy of Finland (AKA) and the Finnish National Fund for Research and Development (SITRA) (Benedictus et al. 1999).

TEKES reports to the Ministry of Trade and Industry and is responsible for the promotion of industry-oriented and applied research. Even though TEKES' funding policy is company oriented, public research institutions received in 2001 42 % of the total funding[26]. Industry-university collaboration was a prerequisite for applications in the period 1994 to 1998 (Enzing et al. 1999). The Academy of Finland (AKA) reports to the Ministry of Education and holds the responsibility of promoting fundamental scientific research. In 2001 14 % of the government R&D expenditure was assigned by the Academy. This funding went primarily to university institutes (82 %) and research centres (8 %). Finally, SITRA is a semi-governmental organisation under the National Bank of Finland. Its duty is the stimulation of company creation and business development through financial support.

According to Enzing et al. (1999, p. 28) the total budget for biotechnology research and development amounted 286,4 million € between 1994 and 1998[27]. The same source reports that about 25 % of the total budget was allocated through public promotion programmes designed by TEKES and AKA, explicitly targeting the development of biotechnology-related research. In the period 1994 to 1998 86.4 million € were invested in biotechnology R&D through specific programmes. This represents about 30 % of the total public R&D investments in biotechnology for the same period.

A5.2.1 Creating and sustaining a biotechnology knowledge base

Policy instruments explicitly targeting biotechnology research were first implemented in Finland in 1988 with the umbrella national "programme for the development of biotechnology and molecular biology". The initiative (divided in three sub-programmes[28] along 1988 and 1996) puts emphasis on the promotion of basic research in strategic biotechnology areas, on the improvement of graduate and post-

---

26 The share has remained relatively constant since 1997 (42 %).

27 The source does not have any figures for the total investment in R&D in the country.

28 The first sub-programme run between 1988 and 1992 and the second sub-programme between 1993 and 1996. The third phase was designed to put additional emphasis on some aspects and run from 1994 to 1996 (Benedictus et al. 1999). According to Tulki et al. (2001) the National programme was extended later on until the year 2000.

graduate training, and most importantly, on the centralisation of research to a limited number of research centres.

Accordingly, the national programme set up the framework for the creation of a network of centres of biotechnological expertise (the so-called *Biocentres* with a budget of 60 million € for the period 1988 and 1996 from the Ministry of Education). Four *Biocentres* were established in those universities which were assessed as having the capacity to develop biotechnology (Helsinki, Turku, Oulu and Kuopio). The relevant institutes at the different universities were concentrated under these umbrella centres. According to Tulki et al. (2001) the establishment of *Biocentres* continued along the 1990s. Two new centres for biotechnology research were established in Tampere and an additional one in Helsinki. This policy instrument was very controversial since it gave strong focus to regional development decentralising limited R&D resources. No more *Biocentres* are planned for the near future (Tulkki et al. 2001).

Both, the Academy of Finland and TEKES were involved in the implementation of the national programme by designing top-down technology programmes for specific biotechnology fields and targeted open calls for proposals with a 9.5 million € budget per year for the period 1988 and 1996[29].

The Academy of Finland (AKA) launched between 1994 and 1998 three programmes promoting biotechnology research with a budget of 12 million €[30]. Besides, together with TEKES, the Academy of Finland developed and financed 3 further programmes[31] allocating about 8 million €. In 2000, together with TEKES, the Academy launched the most important research programme in the field of bio-sciences (Research Programme on Biological Functions of Life 2000, with a budget of 14 million € for 3 years) and the Technology Programme Drug 2000.

The first biotechnology programme supported by TEKES run between 1988 and 1992. Between 1992 and 2000 the centre co-ordinated five biotechnology programmes (2 of them co-financed with the Academy of Finland)[32]. Today, the starting point in designing the programmes is TEKES' technology strategy where bio-

---

29 This budget includes some of the programmes discussed below.

30 The genome research programme (1994-2000); The programme for the reproduction and cultivation of fish (1994-1998); Programme on molecular epidemiology and molecular evolution (1997-1999).

31 National Programme on Materials and Structure Research (1994-2000); Cell Biology Research Programme (1998-2001); Research Programme for Biodiversity (1997-2002).

32 Cell Biology Research Programme* (1998-2001); Research Programme for Biodiversity* (1997-2002); New Generation Paper Technology (1992-1996); Innovation in Foods (1997-2000); Marketing Molecules (1997-2000). *(*) co-financed by the Academy of Finland*

technology has become one of the three fields of priority[33]. Of the 49 ongoing programmes in 2002, six programmes are explicitly supporting biotechnology-related fields (2 of them co-financed with the Academy of Finland)[34]. Even though exact figures of funding of biotechnology through technology programmes of TEKES are not available for the period 1994 to 2001, the increasing number of programmes targeting biotechnology research confirms the attention biotechnology has gained in its funding strategy[35].

Training and education in biotechnology-related fields has been supported at the postgraduate level. Educational investments have been directed specially to postgraduate degrees in medical sciences. Parallel to the creation of the *Biocenters* 14 graduate schools have been established (Tulki et al. 2001).

A5.2.2 Commercialising biotechnology

To support commercialisation of biotechnology the Finnish policy system has concentrated firstly on the creation of the *Biocentres* and secondly on building up technological capabilities for the industry via financial support for business R&D projects.

According to Tulki et al. (2001) the *Biocentres* were established to support links between regional enterprises and local universities. They were also expected to support firm creation and to establish an stimulating environment for innovation in existing companies. However, the scientific specialisation and the industry orientation of the *Biocentres* differs across the locations (Lähteenmäki 2002). The support for commercialisation activities is not homogenous among the *Biocentres* neither. Specially in the city of Turku the "Biocity" is explicitly market oriented and TEKES supports facilities for start-up companies.

Grants for industrial research are the other major policy instrument to build up the technological capabilities of the industry. The technology programmes of TEKES are firm oriented in the sense that they consider the companies' needs as a point of

---

[33] The other two priority fields in the Technology Strategy of TEKES are Information and Communications Technology and Material Technology (TEKES 2001)

[34] Diagnostics 2000 (2000-2003); Drug 2000* (2001-2006), Innovation in Foods (2001-2004); Life 2000 Biological Functions* (2000-2002); NeoBio** (2001-2004); Novel Biotechnology (2001-2004); Structural Biology* 2000-2002 *(*) co-financed with the Academy of Finland, (**) co-financed with SITRA.*

[35] Biotechnology and chemical technology in 2000 received 27 % of TEKES funding (TEKES 2000, p. 5). This share includes technology programmes and funding allocated through open call mechanisms. Figures for biotechnology alone are only available for the year 1998 (11 % of the total budget). The priority of biotechnology for TEKES can only be estimated with the increasing number of programmes targeting biotechnology-related research.

departure. However, the planning takes place in workshops not only involving firms but also universities and research organisations. In 1999 collaboration was not a condition to get funding, however according to TEKES, companies were involved in almost all the public research projects and a large share of the business projects (between 75 % and 85 %) use expertise of public research institutes in the form of bought-in services (TEKES 1999, TEKES 2000). Internationalisation of the research activities within Europe is important for TEKES and collaboration with US and Japan has become important since the late 1990s.

Commercialisation of biotechnology has been supported through horizontal instruments as well. The Finnish policy system has put special attention on the creation of incubators for technology-based start-ups and on the establishment of mechanisms to support the industrial use of scientific research results.

Regarding the establishment of incubators, the European Trend Chart on Innovation (Lemola et al. 2000) emphasises how Finland has followed this approach to encourage start-up of technology-based companies since the late 1980s. In the mid-1990s there were about 15 incubator platforms in Finland. Around the *Biocentres* these infrastructures have supported university-spin-of and start-ups in the biotechnology industry (Benedictus et al. 1999).

The National Fund for Research and Development (SITRA) has been involved in the establishment of six technology transfer institutions in university cities[36]. Licentia Oy, in the city of Helsinki, is one of the most important applicants of biotechnology-related inventions in Finland. Further, the Foundation for Finnish Inventions offers advisory services and financial support for scientists and SMEs to develop and exploit inventions. Finally, innovation centres have been established at universities as separate units to take care of supporting patenting and licensing activities of the university's research units.

A5.2.3 Creating a supportive framework for biotechnology

Regulations general

Biotechnology activities in Finland are governed by three Boards: the Board for Gene Technology, the Board of Novel Food, the Advisory Board of Biotechnology.

- The Board for Gene Technology was created in 1999. The board is appointed by the Council of the State every five years. Its duty is to promote the safe and ethically acceptable use of gene technology and to process notifications concerning

---

[36] Oy AboaTech Ab (in Turku), Licentia Oy (in Helsinki), OuluTech Oy (in Oulu), Tuotekehitys Oy Tamlink and Finn-Medi Tutkimus Oy (in Tampere), Innokarelia Oy (in Lappeenranta

the use and release of genetically modified organisms as defined in the European directives 90/219/EEC, its amendment 98/81/EEC and 90/220/EEC.

- The Board of Novel Food evaluates the novel food products conforming to the EU's Novel Food Regulation (258/07/EY).
- The Advisory Board of Biotechnology is appointed by the Council of the state every three years. It does not give legally binding decisions, is a consultative body, publishes a journal to improve the public understanding of biotechnology and organises debates and seminars related to the field.

The Finnish Gene Technology Act (377/1995) and Decree (821/1995) were adopted in 1995. They present the legislation concerning genetically modified organisms (GMOs) and have been gradually amended in line with the relevant EU Directives on the contained use of GMOs (90/219/EEC) and on the deliberate release of GMOs (90/220/EEC).

Intellectual property rights

Two major IPRs' issues are important for the actors conducting biotechnology research: the legislation on the IPRs of university inventions and the transposition of the 98/44/EG European directive on Legal Protection of Biotechnological Inventions in national law.

According to the law on employment invention (656/67) from 1967 professors and researchers at universities own the intellectual property associated with their own results[37]. The discussions on the modification of the law started in 1998. According to Niskanen et al. (2001) the Finnish Ministry of Education set up a committee in 1998 to clarify the problems related to the IPR legislation in the university sector. The committee recommended to match IPR legislation at universities to the ones in the private sector. However, due to divergent views of the stakeholders no amendments of the law were introduced.

Regarding the 98/44/EG European directive on Legal Protection of Biotechnological Inventions, the directive has been transposed into Finnish national law.

Financing

Measures to promote financial capital investments in high growth sectors have been directed to support venture capital markets and to provide soft loans for business R&D projects.

---

37 Researchers supported by the Academy of Finland and working at state research institutions and the polytechnics do not enjoy this privilege.

The Finnish venture capital market has traditionally been underdeveloped. In the 1990s the Finnish National Fund for Research and Development (SITRA) has strongly supported capital investments in technology-based start-up companies. According to Tulki et al. (2001) in 1991 SITRA's biotechnology investments amounted to 1.2 % (67,000 €) of the total investments. In 2001 biotechnology was the strongest supported industrial branch accounting 9.5 % of SITRA's investments. Further, the same source reports that in 1997 two special funds were created (Sitra Bioventures Ky and Sitra Bio Fund Management Ltd.) with a capital of 25,2 million € to support biotechnology venture capital investments. According to Wess (2002) in 2002 SITRA is a share holder in about 50 companies in the biotech, foodstuffs, chemical, pharmaceutical and diagnostics fields. The same source reports that in 2002 five of the 30 venture capital firms active in Finland focus on biotechnology industry. SITRA estimates that 95 % of the venture capital invested comes from SITRA and the Bio Fund Management Ltd.

Regarding the programmes offering capital and industrial loans[38] for business R&D projects TEKEs' equity loans for companies' product development activities and Finnvera Small Loans Programme have been introduced in the second half of the 1990's[39].

Socio-economic issues

The Finnish policy system uses TEKES technology programmes to promote research related to the socio-economic and ethical aspect of biotechnology.

Further public initiatives related to the socio-economic and ethical aspects of biotechnology have been the creation of three major national ethics committees since 1998: the Board for Gene Technology, the Advisory Board for Biotechnology, and the Advisory Board on Health Care Ethics. In addition to the national committees, there is a wide network of regional and institutional ethics committees, especially in the field of biomedical research and animal research.

Human capital

There seems to be a serious problem of the availability of qualified personnel to carry out the R&D activities of the actors involved in biotechnology research. Problems relate to staffing research positions requiring skills in both scientific and managerial fields. Most actors rely on foreign qualified staff. The creation and development of companies profited very much from the reorganisation Finnish phar-

---

[38] Capital and industrial loans differ in the conditions imposed to pay back the loans.

[39] Finnvera plc is a financing company, owned by the Finnish state. It was created in 1991 and offers financing services to Finnish companies from the start-up phase.

maceutical companies went through in the early and mid 1990's. SMEs had key management and scientific positions with personnel coming from the pharmaceutical sector[40]. Beside the shortage of highly qualified scientific staff there is a lack of students oriented to mathematics and natural sciences in their matriculation examination, too (Schienstock & Tulkki 2001).

Market size

An important disadvantage for Finnish biotech companies is the small size of the Finnish market. That's why the companies have to be globally oriented from the very beginning. However, the lack of management capacities hinders companies to establish themselves on foreign markets (Schienstock & Tulkki 2001).

A5.3 Performance of the Finnish biotechnology innovation system

A5.3.1 Performance related to scientific activities

The absolute number of publications in the field of biotechnology increased noticeable in the last years. Comparing the periods 1990 to 1995 and 1996 to 2001 the number of publications doubled. In the first period 1,508 and in the second period 3,391 biotechnological articles were published by Finnish actors. There is also a significant increase of publication in relation to the number of inhabitant. Between 1990 and 1995 299 publications per million capita were made in Finland and between 1996 and 2001 publishing intensity increased to 658 publications per million capita. Compared to the European average (136 publications per million capita in the first period and 318 publications per million capita in the second period) the Finnish biotechnology system performs very well. In order to get an indication of the efficiency of the research system, publication output is also related to the number of researchers[41]. In the first period publication intensity related to the number of researchers amounted to 98 per thousand researchers, which was clearly above the European average of 65 publications per thousand researchers. In the second period publication intensity increased substantially to 141 publications per thousand researchers, compared to an EU level of 137. Taken together, publication indicators point to a very good performance of the Finnish biotechnology innovation system.

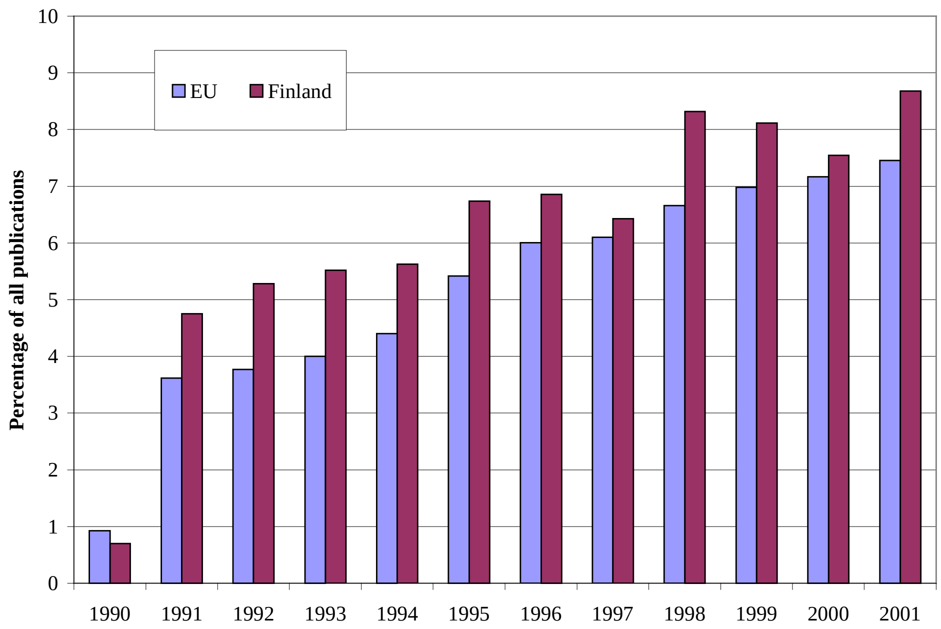
In addition, the percentage of biotechnology publications of all Finnish publications provides an indication for the significance of biotechnology in the Finnish research

[40] Schienstock et al. (2001) point out this influence as well.

[41] Since official data on the number of researchers in biotechnology are not available, we use the OECD figures for all researchers in the country.

system. The share of biotechnology publications increased between 1990 and 2001. In 1990 less than 1 % of all publications were connected with biotechnology. In 2001 8.7 % of all were biotechnological publications. Since 1991 the share of biotechnology publications in Finland was much higher than the average numbers for Europe (figure A5.1).

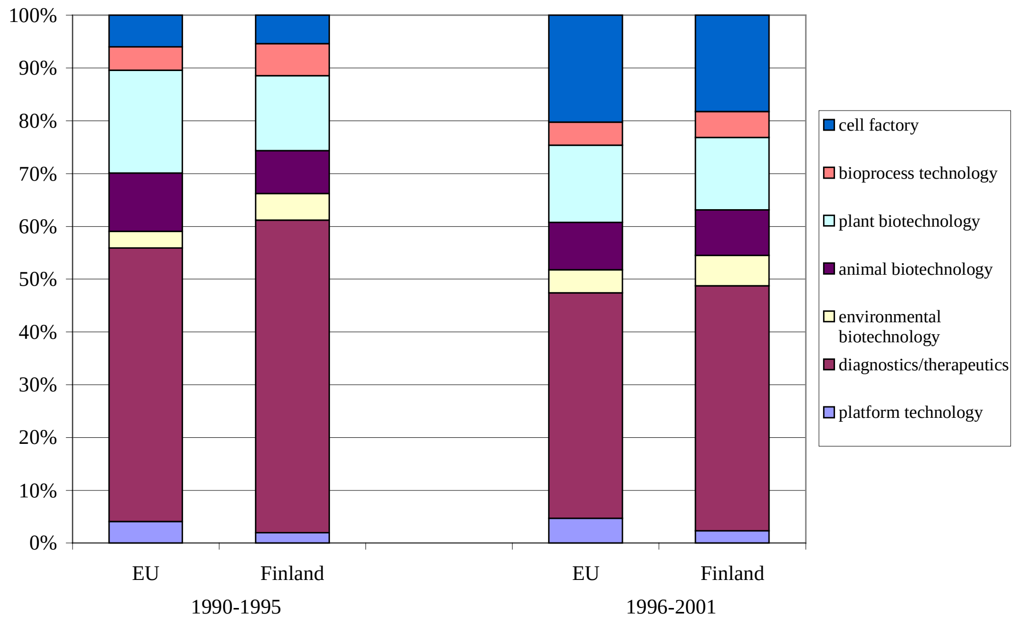
Figure A5.1: Share of publications in the field of biotechnology of all publications in Finland



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

The biotechnological profile on basis of the biotechnological publications shows the field of diagnostics and therapeutics as the most important research area in Finland. Especially in the first period between 1990 and 1995 publications in this field were dominant (more than 59 % of all biotechnological publications). Diagnostics and therapeutics were also important in the period from 1996 to 2001 with 46 % of all publications. Another important Finnish research area is plant biotechnology (14 % in both periods). Bioprocess technology and environmental biotechnology are two fields, in which the percentage of publications go beyond the European average (figure A5.2).

Figure A5.2: Share of different biotechnological fields in the Finnish biotechnology compared with the EU



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

A5.3.2 Performance related to commercialisation

Biotechnological firms

Two thirds of the Finnish biotechnology industry are concentrated in the Helsinki and Turku regions. Other regional centres are located in Kuopio, Oulu and Tampere. Table A5.1 shows that the number of biotech companies in Finland amounts to 77 in the year 2000.

Table A5.1: Number of biotechnological firms in Finland

	1996	**1997**	**1998**	**1999**	**2000**
Number of biotech firms	30	46	51	74	77

Source: Ernst & Young

74 % of the biotech companies were founded after 1991. The median creation date of the firms is 1994. Especially the younger firms are small or very small and have less than 50 employees. While the oldest firms concentrate their activities on diag-

nostic, the younger firms were active in pharmaceuticals, diagnostics and food and feed (Hermans & Luukkonen 2002).

Venture capital invested in biotechnology

Table A5.2 shows the amount of venture capital that has been invested in Finnish biotechnology between 1990 and 1995 as well as between 1996 and 2000. In the second period venture capital invested in biotechnology companies amounts to 32.7 million €. In absolute figures the amount has increased nearly eight times, and also in relation to the biotechnology venture capital in the whole EU a twofold increase can be found.

Table A5.2: Venture capital invested in Finnish biotechnology

Year	**absolute value**		**% of venture capital invested in EU**
	in 1,000 €	in 1,000 PPP[42]	
1990 to 1995	4397.43	3752.803	0.86
1996 to 2000	32684.26	30017.623	1.68

Source: EVCA

As table A5.3 indicates, the amount of biotechnology venture capital increased not only in absolute figures, but also relative to the mean population nearly eightfold in Finland and goes clear beyond the EU level.

Table A5.3: Indices of venture capital invested in Finland

	Finland		**EU**	
Year	**absolute amount**	**amount relative to mean population**	**absolute amount**	**amount relative to mean population**
	in 1,000 PPP	in PPP per inhabitant	in 1,000 PPP	in PPP per inhabitant
1990 to 1995	3752.803	0.743	438919.599	1.191
1996 to 2000	30017.623	5.826	1783683.684	4.760

Source: EVCA

42 PPP: purchase power parity

Initial public offerings

BioTie Therapeutics was the only biotechnology company in Finland which went public between 1995 and 2000. Its initial public offering (IPO) took place in 2000[43].

Drugs approved

According to data from EMEA no bio-medicines originating from Finnish companies were approved by EMEA between 1995 and 2001.

Field trials of GMO plants

18 field trials of GM plants were notified to the EU. Table A5.4 shows the number of approved notifications per year.

Table A5.4: Approved notifications of field trials with GMOs in Finland per year

	1996	**1997**	**1998**	**1999**	**2000**	**2001**
approved notifications	5	6	1	3	2	1

Source: ICHP 2002

The field trials were notified for the following plants: sugar beet (5), birch (4), oilseed rape (3), potato (3), barley (2), pine (2), spruce (2) and one field trial each for broccoli, cabbage, cauliflower and tobacco. The Finnish notifications were carried out by public research (11), large firms (5), universities (4) and SME (2) and account for 1.1 % of all field trials in the EU.

Patent applications

Between 1990 and 1995 Finnish actors applied for 151 patents for biotechnological inventions and between 1996 and 2000 for 141 patents[44]. Most of the Finnish biotech patents came from the subfields of diagnostics/therapeutics, platform technologies and bioprocessing technologies. In recent years the number of patents increased especially in the subfield of platform technologies whereas the patent number decreased in the subfield of diagnostics.

[43] Sources: E&Y Annual European Life Sciences Reports, websites by Nasdaq, Neuer Markt, London Stock Exchange, Euronext

[44] The patent numbers for the year 2000 are estimated.

Patenting intensity related to population decreased slightly from 29.9 biotechnology patents per million inhabitants in the first period to 27.4 patents per million inhabitants in the second period. But both values are above the European average of 16.2 (first period) and 25.3 (second period). Patenting intensities related to researchers decrease from 9.8 biotechnology patent applications per thousand researchers in the first period to 5.9 patent applications per thousand researchers in the second period. The first value is above and the second below the European average of 7.8 (first period) and 10.9 (second period).

The share of biotechnology patents of all patents in Finland was 4.3 % in the first period of investigation and decreased to 2.7 % in the second period. Compared to the European situation with a biotechnology share of 3.4 % (first period) and 4.5 % (second period) biotechnology Finland fall back behind the EU values in the 1996 to 2000 period. Obviously, other sectors are patenting more intensively in Finland than biotechnology.

A5.4 Conclusions

Since the beginning of the 1990's support for R&D and commercialisation of Biotechnology is a policy priority in Finland. In the period 1994 to 1998 instruments to support biotechnology focused on the concentration of biotechnology basic research in regional (biotechnology-specific) research centres (*the Biocentres*). Besides, biotechnology has cashed in from competitive funding mechanisms for university research and industrial grants and loans for the business sector. Since the mid 1990's the policy system has increasingly introduced top-down approaches targeting biotechnology research and development. Further, the government has put emphasis on supporting the availability of financial capital for the creation of technology-based companies.

The performance analysis of the Finnish biotechnology innovation system indicates that Finland is a strong producer of knowledge in biotechnology-related fields, however, the slowing-down of growth rates of publications in biotechnology during the 1990s seems to indicate that the dynamics of knowledge production is decreasing. Commercialisation of biotechnology has been very successful in terms of biotechnology companies created and venture capital raised. Similar to the scientific performance the intensity of patenting activities in biotechnology seems to decrease in the late 1990s which can be interpreted as an early warning signal for potential future problems in the further development of the sector. Additional problems are emerging with respect to supplying qualified staff and enlarging the knowledge base. Concerning commercialisation the unbalance between company creation and patent performance dynamics points to additional potential problems.

A6 Biotechnology innovation system in Germany

A6.1 Introduction

Germany has a population of 83.1 million people. Its economy has developed from the primary and secondary sector to the third sector in the last decades. More than two thirds of all German employees work in the services sector. Areas like trade, traffic or service for companies, financing and insurance and government count to this sector. For years the state was the most important employer, but since mid of the 1990th the employment by the state is declining. 29 % of all employees are employed in industry. Only 2.5 % of all employees work in agriculture and forestry.

According to figures of the OECD (2002) the gross domestic expenditure on R&D (GERD) amounted up to 52,851.1 million PPP in 2000. This corresponds to a ratio of 2.48 % GDP which is clear above the EU average of 1.88 % and also above the OECD average of 2.24 %. The German GERD share in the GDP increased since 1996. GERD per capita population was 643 PPP in the year 2000 which is much more than the European average of 457.7 PPP in the same year. Since 1996 per capita GERD increased continuously in Germany and reached a level of 668.4 PPP in 2001. 66.1 % of GERD was financed by industry in the year 2000. This share shows that the industry contribution to R&D financing in Germany exceeds the corresponding shares for the European Union (55.5 %) and for the OECD (62.9 %). The industry contribution to GERD increased since 1996. The total number of German researchers was 255,260 (full time equivalent (FTE)) in 1999. This corresponds to a ratio of 6.7 % per thousand total employment which is clear above the European value of 5.6 % and slightly above the OECD ratio of 6.6 % in the same year. In sum, these indicators show that in terms of input to R&D Germany ranks above the European average.

The following chapters will characterise the German innovation system in the field of biotechnology. The first chapter will describe the policy framework supporting biotechnology in Germany, the performance of the German biotechnology innovation system will be discussed in the second chapter. Finally, conclusions on how different policy instruments contributed to shaping the present situation of the German biotechnology innovation systems will be drawn.

A6.2 Policy framework

Germany did not introduce specific programmes for biotechnology until the second half of the 1980s. A report about biotechnology was commissioned in the early

1970s and funding some biotechnology projects started at that time. The first larger infrastructural measure to build up the science base was the establishment of Gene Centres in Cologne, Heidelberg and Munich in 1982. The first programme for promoting "applied biology and biotechnology", however, commenced only in 1985.

The German funding system is characterised by the large number of actors and ministries involved at the regional and federal level and the variety of instruments implemented. Between 1994 and 2001 at the national level four Federal Ministries ('Education and Research', 'Environment', 'Food, Agriculture and Forestry' and 'Economics and Technology') together with the German Research Council (DFG) have been directly or indirectly involved in supporting the development and commercialisation of biotechnology. The federal system confers the federal states the possibility to participate in the funding process. Hence, promotion activities at the regional level are also important in the biotechnology funding system[45] (Enzing et al. 1999).

Mainly the biotechnology division of the Federal Ministry for Education and Research (BMBF) has been responsible for implementing public promotion programmes explicitly targeting the development and commercialisation of biotechnology. According to the Public Promotion Catalogue of the BMBF[46] the share of public funds directed to biotechnology R&D activities in 1994 amounted to 1.9 % of the total R&D expenditures[47]. The share has gradually increased reaching a 2.4 % in 1998 and a 3.2 % in 2001. The two main instruments to allocate the public funding are direct project funding and institutional funding. In 1994, 57 % of the funding was allocated through direct project funding. In 2001 this share reached 70 %. Industry actors have gained importance in the funding activities of the ministry. In 2000 23 % of the biotechnology investments of the BMBF were granted to industry actors (in 1993 the share was 13 %).

Giessler et al. (1999) estimate an annual federal budget for biotechnology (including project and institutional funding) of 604.3 million ECU per year between 1994 and 1998. Regarding the promotion of the different biotechnology fields public promotion programmes for R&D and related activities focused on "Development of basic biotechnology", "Plant biotechnology", and "Human or veterinary diagnostics".

---

45 For a short review of the programmes and budgets of the German federal states in 1994 and 1995 see Giessler et al. 1999

46 FöKat (Funding catalogue of the Federal Ministry for Education and Research, September 2002) http://oas.ip.kp.dlr.de/foekat/foekat/foekat

47 This figure includes only the investments classified as biotechnology activities by the BMBF and does not consider expenditures in medical, health and environmental research that may directly support biotechnology research as well. The same accounts all for the shares presented in the paragraph.

Biotechnology research is carried out by universities and, specially, by the Helmholtz research centres and the research institutes of the Max Planck and Fraunhofer Societies. Industry actors have increased their involvement in biotechnology research and commercialisation very rapidly in the last decade changing the institutional structure of the German Biotechnology system considerably.

A6.2.1 Creating and sustaining a biotechnology knowledge base

Giessler et al. (1999) identify three promotion programmes supporting the biotechnology knowledge base in Germany between 1994 and 1998. These are the Biotechnology 2000, Environmental Research and Environmental Technology and the Health 2000 programmes. The Biotechnology 2000 programme (launched in 1990 and replaced by the follow-up Biotechnology frame work programme") defines the framework for direct promotion of biotechnology activities in Germany. Other key initiatives designed explicitly to promote biotechnology research have been the German Human Genome Project (launched in 1995), the associative project Genome Analysis of the Plant Biological System (launched in 1999) and the National Genome Research Network (launched in 2001).

Already in 1990, the Federal Ministry of Research and Education put special emphasis on collaborative research and on the commercial application of the research results of the projects to be funded. The Biotechnology 2000 programme granted 50 % of the yearly budget for project funding (BMFT 1990). To allocate the funding the ministry supported public and industry research units organising their research projects as "linked" and "lead" projects (*Verbund- und Leitprojekte*). These projects had to be carried out by research consortia that included an industrial partner and, most importantly, expected research results of industrial interest. This instrument was explicitly directed to stimulate collaborative research and the involvement of industry actors in the public research activities.

In June 1995 with the German Human Genome Project the ministry, together with the German Research Council, launched a key initiative for the support of basic research around the human genome. In 2000 the initiative entered its second phase. Most of the funded projects have been allocated to national research centres (Helmholtz-Centres) and Max Planck Institutes in the form of "linked" projects. A resource centre has been established to gather and co-ordinate the information and the scientific results of all the projects. Companies are very involved and play an important role in the project.

Another example of the promotion of collaborative research and industrial orientation of the research activities is the associative project Genome Analysis of the Plant Biological System (GABI) that was launched in 1999 for eight years. The support of basic research was an explicit goal of the project. Again industry actors (represented by the 'Economic Association Plant Genome Research GABI e.V.') are very involved in the programme by carrying out research and by financing it partly. The research projects are divided in to two areas: basic research projects and application-oriented research projects with different funding conditions.

In 2001 the Federal Ministry for Research and Education (BMBF) decided to increase its funding of human genome research substantially by establishing the National Genome Research Network. One main characteristic of the network is its interdisciplinary character, thus it combines efforts on genome research with medical research on the genetic basis of diseases[48].

Most health- and biotechnology-related basic research is funded through mechanisms that do not explicitly target the development of biotechnology. These include institutional support for public research organisations (like universities, Helmholtz Research Centres and Institutes of the Max Planck and Fraunhofer Societies) and the competitive open call system of the German Research Council (DFG) to finance university research. Through this type of funding the research organisations can preserve their autonomy, and accordingly design and implement their research projects independently from any policy interests and framework programme of the Federal Ministries.

A6.2.2 Commercialising biotechnology

The first approach to support commercialisation in biotechnology is the implementation of mechanisms to promote biotechnology research of industry actors. This should be achieved by stimulating the involvement of industry actors in biotechnology research activities conducted in collaboration with public research organisations (see above). On the other hand, the Gene Centres should improve the access of the industry to scientific and technological capabilities. Between 1982 and 1995 140 million € were invested for this goal.

Since the 1980s a specific form of project funding for small and medium-sized enterprises has been developed, the so-called indirect specific promotion of R&D. The aim of such measure is to support the diffusion of innovative technology into various sectors. The measure concentrates on specific technologies such as biotechnology. In order to motivate small and medium-sized firms to participate in such programmes, the administrative hurdles are set relatively low and the application and approval procedures are fast. For example, it is not necessary to formulate lengthy scientific proposals. However, firms need to show that they have the capabilities and capacities to carry out the project and they are also expected to contribute at least 50 % of the project budget. In the early 1990s these programmes have been

[48] With the Biotechnology Framework Programme launched in 2001 other network and thematic programmes were designed to support the knowledge base. This section has summarised only the instruments that present new policy approaches.

quite successful by motivating several hundred small and medium-sized firms to use biotechnology.

Secondly, instruments for commercialisation support of biotechnology included initiatives for cluster formation. The BioRegio contest (1995 to 2001) was an important policy instrument implemented within the Biotechnology 2000 programme. The initiative was designed as a competition where regions with the most convincing network projects were awarded with large amounts of public funding. A major intention was to promote and accelerate the transfer of biotechnological know-how into products, processes and services by supporting regional interaction between research units, financing institutions and industry actors. The follow-up programme BioProfile (1999 to 2006) can be considered as an extension of the BioRegio contest.

Finally, special emphasis has been given to structural measures to support creation and development of start-ups in biotechnology-related fields and technology transfer mechanisms. Direct support to company creation in the biotechnology field is given by the BioChance initiative launched in 1998. The programme supports high risk research projects of biotechnology start-ups. Funds for technology transfer institutions were also included in the BioRegio and BioProfile initiatives.

Promotion measures for industrial research and for the application and commercialisation of technologies are also responsibility of the Federal Ministry of Economic Affairs and Communication and Technology (BMWi, now Federal Ministry of Economic Affairs and Communication and Labour – BMWA) who reserves funding for industrial research and supports the AiF (German Federation of Industrial Cooperative Research Associations "Otto von Guericke" e.V.) The AiF has an annual budget of nearly 250 million € of public funds. In 1994 AiF biotechnology project funding amounted to about 35 % of the total budget (Giessler et al. 1999).

Technology transfer mechanisms for public sector research are well developed in Germany. The support for commercialisation of scientific results has been implemented at federal and regional level through various technology transfer mechanisms and the support for university spin-offs, specially in biotechnology-related fields[49].

---

[49] These are some of the major initiatives: (1) Establishment of Agencies for Technology Transfer and Innovation Promotion (Agenturen für Technologietransfer und Innovationsförderung, ATI), Technology Transfer Centres (TTZ) and AN-Institutes (Technology Transfer Institutes at Universities); (2) the INSTI project launched in 1995 by the Federal Ministry of Education and Research to provide SMEs with access to the scientific-technical information gathered in patent documents and Patent Information Centres (PIZ) were established; (3) Since 1999 and until 2003 the Programme INNONET aims at promoting innovative networks and the exchange of R&D staff between business and research institutes; (4) in 1999 the Ministry for Education and Research initiated the InnoRegio competition for the creation of regional clusters of companies, institutions and research institutes in the Eastern states of Germany; (5) since 2001 the initiative

A6.2.3 Creating a supportive framework for biotechnology

Regulations general

The "Genetic Engineering Act" of 1992, regulations on the use of genetically modifies organisms (GMO) and the existing Embryo Protection Act establish the regulatory framework in Germany to conduct biotechnology research.

With the "Genetic Engineering Act" Germany was one of the first industrialised nations introducing a law to regulate genetic engineering. In December 1993 an amendment of the "Genetic Engineering Act of 1992" abolished some restrictions and bureaucratic obstacles (Woerner et al. 2000). The government has declared the intention of transposing the European directive 90/220 of the Deliberate Release of GMOs updated in February 2001 and the Contained-use-Directive 98/81 (EU) into national law. Concerning research with stem cells, current legislation bans the import of human embryonic stem (ES) cells and allows research on the cells under strict conditions permitting work only with stem cell lines created before 30 January 2002 and only if a researcher can demonstrate no feasible alternatives.

Intellectual property rights

The German legislation on IPR is going through gradual modifications changing the framework conditions for the development of biotechnology. The main issues are the legislation on university patents and the legal protection of biotechnological inventions.

In 2002 the regulations on ownership of university patents was changed. Accordingly, since February 2002 all inventions have to be presented to the research institution which has to proof the convenience of applying for intellectual protection. The institution can decide whether it wants to apply for patent protection or leave them to the inventor for application. Inventors receive 30 % of the compensation profits. Before this amendment university teachers owned patents and universities had no means to achieve control over university inventions.

Regarding the 98/44/EG European directive on Legal Protection of Biotechnological Inventions, the directive has not been transposed into German national law. In June 2001 the directive was in the final stage of the process of being transposed into national law. However, the transposition process failed.

"Knowledge creates markets" reserves funding to support the establishment of a professional patent and commercialisation agencies. This aims to promote the exploitation of research generated at facilities, which do not have the necessary commercialisation expertise in-house; (6) EXIST – start ups from science (1998-2001) provides 7.5 million € per year to improve entrepreneurship and knowledge spill-overs from academics to industry.

Financing

The improvement of the financing conditions of technology-oriented start-ups has been supported since the early 1990s through public early stage venture programmes to stimulate the venture capital market. After the TOU-NBL[50] initiative for the new federal states (1990 to 1995) and the pilot promotion project BJTU[51] in 1994, the first nation-wide programme for technology-oriented start-ups BTU[52] (Business Investment Capital for Small Technology-Based Firms) was launched in 1995. The BTU programme offered two models of support: the "DtA co-investor model" and the "KfW refinancing model". Both models aiming at reducing the risk of venture capitalists to stimulate start-ups financing in innovative sectors. The instruments to promote business investment capitals continue to be implemented. In 2001 the BTU-Frühphase[53] was launched to support small technology-based firms in the start-up phase.

Other initiatives to stimulate the financing of innovations after 1994 have been the FUTOUR programme (1997 to 1999, extended until 2005) providing public venture capital for firms in the new federal states, in 1997 the creation of the "Neuer Markt" in Frankfurt[54] and in 1998 establishment of the Business Angles Network Germany (BAND).

Socio-economic issues

Driven by the public debate and the conflict between scientific, commercial and public interests, the support of activities and institutions concerned with ethical and socio-economic aspects of biotechnology is gradually becoming more important for the policy system.

Public acceptance

Social acceptance of biotechnology is a very important issue in Germany. Generally the German public discussion is characterised by a rather polarised debate between supporters and opponents. On the one hand there are euphoric estimations and expectations by the German government and some representatives of science and industry. On the other hand there are critical viewpoints, especially from consumer organisations, churches, and environmental groups. In the last years topics like ani-

---

50 *Förderung technologieorientierter Unternehmensgründungen in den neuen Bundesländern*

51 *Beteiligungskapital für junge Technologieunternehmen*

52 *Beteiligungskapital für kleine Technologieunternehmen*

53 *Beteiligungskapital für die Phase der Unternehmensgründung*

54 Which has been re-organised in the wake of the stock market crisis in 2002.

mal testing in the bio-pharmaceutical industry, the risks associated with the production of GMOs, the ethical issues related with the clinical trials, but also stem cell research were under discussion. On the other hand, most medical applications of biotechnology such as new drugs or diagnostics are well accepted by the public.

A6.3 Performance of the German biotechnology innovation system

A6.3.1 Performance related to scientific activities

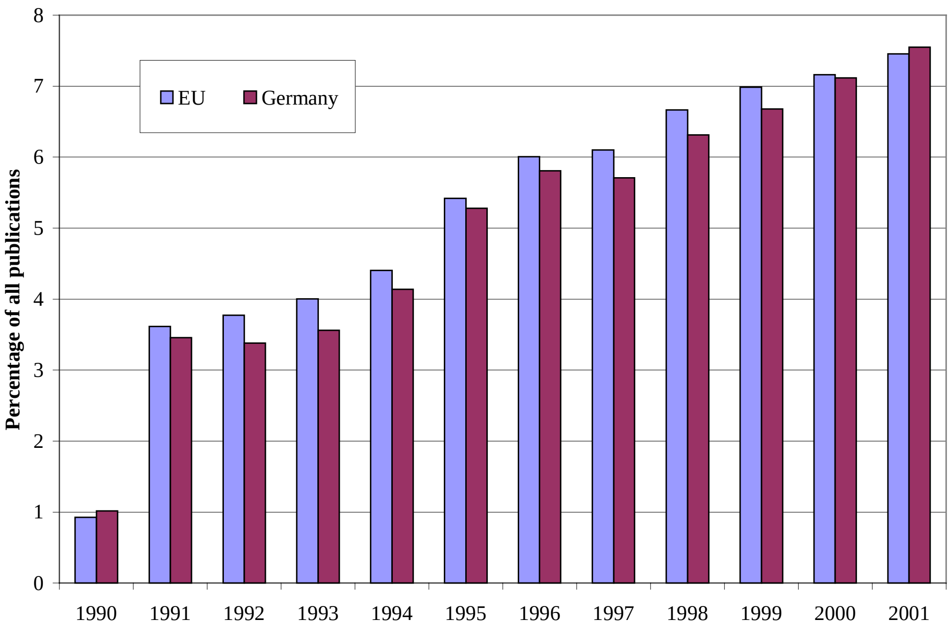
As in other countries the absolute number of publications in the field of biotechnology increased in Germany in the last years. Between 1990 and 1995 10,807 biotechnological articles were published by German actors. This number went up to 27,972 articles in the period between 1996 and 2001. A very significant increase of publication output in biotechnology is also obvious if we relate publications to the number of inhabitants of the country. In the first period (1990 to 1995) 139 publications per million capita were made in Germany. In the second period (1996 to 2001) the number of publications per million capita increased to 341. Compared to the European average (136 publications per million capita in the first period and 318 publications per million capita in the second period), the performance of the German biotechnology system is very close to the average. As an indicator of the efficiency of the research system publication output is related to the number of researchers[55]. In the first period publication intensity related to the number of researchers amounted to 46 publications per thousand researchers, which was below the European average of 65. In the second period publication intensity increased to 115 publications per thousand researchers, which was, however, still below EU level of 137.

Another indicator to assess the significance of biotechnology in the German research system is the share of biotechnology publications of all German publications. The share of biotechnology publications increased from 1990 to 2001. In 1990 only 1 % of all publications dealt with biotechnology. In 2001 7.6 % of all were biotechnological publications. In this context it is noticeable that except the years 1990 and 2001 the percentage of biotechnology publications in Germany remains under the European average in each year (figure A6.1).

---

55 Since official data on the number of researcher in biotechnology are not available, we use the OECD figures for all researchers in the country.

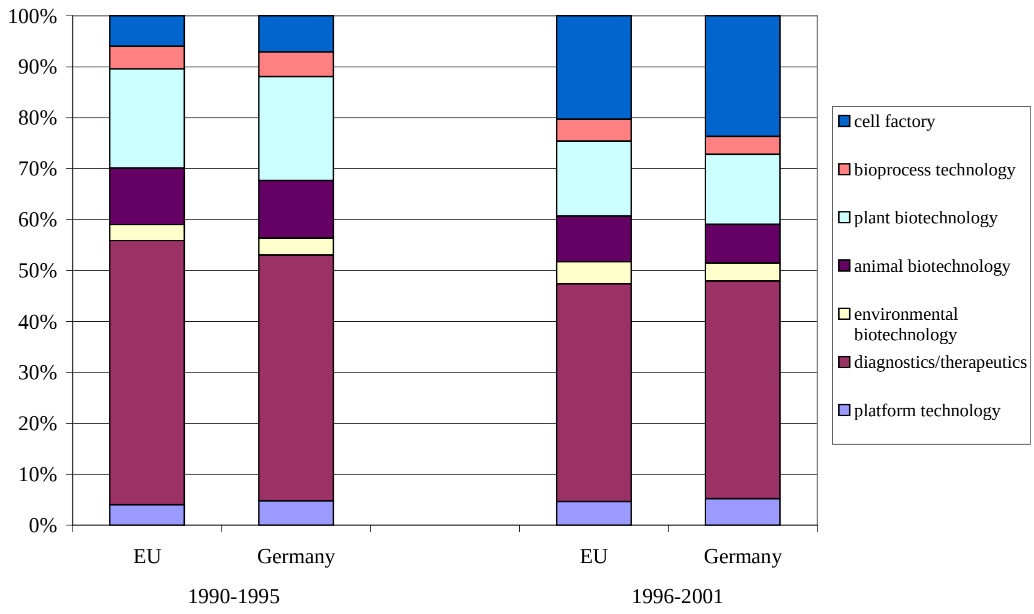
Figure A6.1: Share of publications in the field of biotechnology of all publications in Germany



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

The German biotechnological profile is dominated by diagnostics and therapeutics (48 % or 43 %, respectively in the first and second period) and plant biotechnology (20 % or 14 %, respectively). To a smaller extent also the field of cell factory attract special attention in Germany compared to the EU. But in most fields the German biotechnological profile corresponds with the European profile (figure A6.2), which could be expected due to the large share of German publications in Europe.

Figure A6.2: Share of different biotechnological fields in the German biotechnology compared with the EU



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

A6.3.2 Performance related to commercialisation

Biotechnological firms

On basis of biotechnological firms Germany counts to the leading European countries in the field of biotechnology. In 2001 the number of biotechnological firms increased to 365 (table A6.1) (Ernst & Young).

Table A6.1: Number of biotechnological firms in Germany

	1993	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**
Number of biotech firms	22	73	95	104	175	228	275	330	365

Source: Ernst & Young

Nearly 80 % of these companies are small or very small (less than 50 employees). The median foundation year for firms in Germany is 1994. These results are suggesting that the majority have been created specifically to exploit biotechnology.

The greatest number of German biotech firms are involved in pharmaceutical applications of biotechnology, followed by equipment and supplies firms and firms involved in agro-food biotech applications.

Venture capital invested in biotechnology

There is an abundance of venture capital seeking investment opportunities in Germany, and a high interest in biopharmaceutical firms because of the potential for a high return, especially when a company is launched on the stock exchange.

Table A6.2 shows the amount of venture capital that has been invested in German biotechnology in the two investigated periods 1990 to 1995 and 1996 to 2000. In the latter period around 867.3 million € venture capital has been invested in biotechnology companies. In absolute figures the amount has increased nearly ten times. In relation to the biotechnology venture capital in the whole EU a strong increase from 18 % to 45 % can be found, too.

Table A6.2: Venture capital invested in German biotechnology

Year	**absolute value**		**% of venture capital invested in EU**
	in 1,000 €	in 1,000 PPP[56]	
1990 to 1995	90025.40	79710.557	18.16
1996 to 2000	867324.47	805498.667	45.16

Source: EVCA

As table A6.3 indicates, the amount of biotechnology venture capital increased not only in absolute figures, but also relative to the mean population nearly tenfold in Germany that is twice as much as the EU level.

Table A6.3: Indices of venture capital invested in Germany

	Germany		**EU**	
Year	**absolute amount**	**amount relative to mean population**	**absolute amount**	**amount relative to mean population**
	in 1,000 PPP	in PPP per inhabitant	in 1,000 PPP	in PPP per inhabitant
1990 to 1995	79710.557	0.988	438919.599	1.191
1996 to 2000	805498.667	9.778	1783683.684	4.760

Source: EVCA

Initial public offerings

56 PPP: purchase power parity

There were 17 initial public offerings (IPO) of a biotechnology companies in Germany between 1995 and 2000. The first biotech firm which went public were Qiagen and Biotest in 1996. In 1999 the next five companies went public: Cybio; Evotec OAI; Morphosys; MWG-Biotech; Rhein Biotech. In 2000 the IPO of altogether ten firms took place: LION Bioscience; MediGene; PlasmaSelect; GPC Biotech; GeneScan Europe; Girindus; November; Biolitec; BioTissue Technologies; Curasan.

Drugs approved

Between 1995 and 2001 seven bio-medicines were approved by EMEA: one in 1995, one in 1999, two in 2000 and three in 2001. The German share of approved drugs in whole Europe amounts to 17 %.

Field trials of GMO plants

115 field trials of GM plants were notified to the EU. Table A6.4 shows the number of approved notifications per year.

Table A6.4: Approved notifications of field trials with GMOs in Germany per year

	1992	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**
approved notifications	4	1	13	16	20	19	18	16	3	5

Source: ICHP 2002

The field trials were notified for the following plants: potato (42), oilseed rape (38), sugar beet (26), maize (19), petunia (2), poplar (2), and one field trial each for grape, pea and tobacco. The German notifications were carried out by large companies (53), public research (37), universities (14) and SME (13) and account for 6.8 % of all field trials in the EU.

Patent applications

German actors applied for 1,716 patents for biotechnological inventions between 1990 and 1995 and for 2,653 patents between 1996 and 2000[57] at the European Patent Office. Most of the patents came from the subfields of platform technologies, diagnostics/therapeutics, cell factory and bioprocessing technologies. In the last

57 The patent numbers for the year 2000 are estimated.

years the number of patents increased especially in the subfield of platform technologies where as the patent number decreased in the subfield of diagnostics.

Patenting intensity related to population increased significantly from 22 biotechnology patents per million inhabitants between 1990 and 1995 to 32.3 patents per million inhabitants in the period between 1996 and 2001. Both values are above the European average of 16.2 (first period) and 25.3 (second period). Patenting intensities related to researchers also increase considerably from 7.3 biotechnology patent applications per thousand researchers in the first period to 10.9 patent applications per thousand researchers in the second period. Both values are very close to the European average of 7.8 (first period) and 10.9 patent applications per thousand researchers (second period).

The share of biotechnology patents of all German patents was 2.3 % between 1990 and 1995 and increased to 3 % in the second period. These values were lower than the corresponding values of the EU (3.4 % and 4.5 %), what indicates a relatively low relevance of biotechnology inventions compared to all technological areas in Germany.

A6.4 Conclusions

The S&T indicators applied to evaluate the development of the biotechnology knowledge base in Germany have slightly improved between 1994 and 2001 but present only an average performance in comparison with the other EU countries. On the other side indicators for the commercialisation of biotechnology picture a strong performance even though the recent signals in the evolution of the industry awake concern about the sustainability of the growth experienced.

The concentration of the policy system on the support for the commercialisation of technologies has been clear. Technology transfer instruments and the availability of financial capital for firm creation have been the major policy concerns. Biotechnology-specific measures for commercialisation support were principally the stimulation of industry involvement in biotechnology activities and creation of regional networks. The instruments implemented to support network formation between actors involved in the processes of biotechnology development and commercialisation proved very effective.

The overall results present a mismatch between the evolution of the knowledge base and the commercialisation activities. Even though we cannot conclude that policy is the only responsible for the performance of the German system, the indicators and also assessments of key target groups of different policies speak in favour of the effectiveness of the instruments implanted to stimulate the network formation and the commercialisation of scientific results. However, the moderate performance of the system in the creation of knowledge and the strong dependence of some industry actors on venture capital investments raise some concern concerning the sustainability of the commercialisation activities in the long-term.

A7 Biotechnology innovation system in Ireland

The following chapter gives a brief overview on the Irish biotechnology innovation system. The introduction presents a brief overview of the country including key indicators concerning the general framework conditions for biotechnology innovation in Ireland. The second chapter describes the policy framework for creating and sustaining a biotechnology knowledge base, for commercialising biotechnology and for creating a supportive framework for biotechnology. Chapter A7.3 assesses the performance of the biotechnology sector in Ireland, focussing on the performance related to scientific activities as well as related to commercialisation of products. Chapter A7.4 summarises the current situation and adds conclusions on the effectiveness of policy measures with respect to the main policy goals.

A7.1 Introduction

The Republic of Ireland has a population of 3.5 million people and its economy has traditionally been based on agriculture. In the last few decades the country has undergone a process of rapid modernisation and has developed a strong manufacturing sector, much of it manufacturing plants of foreign companies. National investment in R&D has been historically low, due to both low industrial investment in R&D and the poor funding of research in higher education. In the 1990's, Ireland's small open economy has outperformed all other European economies. According to the OECD, Ireland's economy has grown at an impressive average annual rate of 8.5 % in real terms in the five-year period from 1994 to 1999, compared to an EU average of 2.3 %. This transformation of the economy is the result of several factors, e. g. favourable demographics, substantial inward investment flows, strategic deployment of EU structural and cohesion funds, a social partnership approach to economic development, an openness to international trade in goods and services, effective industrial policy, and an emphasis on education and technological innovation.

Government promotional agencies have selectively targeted particular areas of industry that produce sophisticated and high value products and services offering the best growth potential and the best prospects of generating long-term sustainable employment in Ireland. Targeted sectors in the past have included chemicals, pharmaceuticals, and medical devices. More recently e-commerce, electronics, software, internationally traded services sector, including financial services, call centres and shared services centres, biotechnology and ICT have been the focus.

During the 1990s, EU structural funds were invested in the R&D infrastructure in Ireland. The Irish government also established a set of new institutions to administer the increasing resources being given to research. As a result gross expenditure on R&D (GERD) rose from 1.31 % to 1.39 % of GDP between 1994 and 1997 (OECD 2001). In 1999 – no later data are available for Ireland unfortunately – the percentage of the GDP spent on R&D was 1.21 %, compared to 1.88 % in the EU and 2.24 % in the OECD (EU and OECD data for the year 2000). A relatively high share of 64.1 % of the gross R&D expenditures was financed by the industry in 1999 (EU: 55.5 %; OECD: 62.9 %). Related to the population size, only 312.6 current PPP$ were spent for R&D per capita population in 1999, compared to 457.7 current PPP$ in the EU and 534.8 in the OECD (EU and OECD data for the year 2000).

The Industrial Development Act in the year 1993 created an industrial development agency now known as Enterprise Ireland (EI) with the mission of increasing business investment in R&D and stimulating innovation. A main policy focus is to support indigenous industry.

An important feature of the Irish situation is the presence of US firms doing research in Ireland. Thereby a bigger critical mass of people is created and the available expertise is expanded. Further, researchers from other countries are attracted to work in Ireland. However, in 1998, 5.1 out of thousand employed persons worked as full time researchers in Ireland, somewhat less than in the EU (5.4 per thousand employees) and in the OECD (6.4 per thousand).

A7.2 Policy framework

The main emphasis of the Irish government policy for biotechnology has been to support commercialisation, and it is only since 2001 that the funds for basic research have also been increased substantially. In the following, Irish policy measures targeted at supporting the science base, improving commercialisation and creating supportive framework conditions for biotechnology are summarised.

A7.2.1 Creating and sustaining a biotechnology knowledge base

In Ireland, since the late 1980s and until 2000 there was one main National Biotechnology Programme called BioResearch Ireland (BRI). The most important organisation funding biotechnology research in Ireland is Enterprise Ireland (EI). Its goals are to support industrial R&D and harness the expertise and knowledge of the universities and technical colleges in biotechnology as well as in other fields. It has three main activities:

(1) Direct support of industrial R&D through several schemes including the Research Technology and Innovation Competitive Grants Initiative which gives financial assistance for product and process development. Companies are encouraged to work with public research organisations, but can also use the

funds for in-house research. It allocated 1.15 million € to biotechnology research in the period 1994 to 1998.

(2) Administration of the National Research Support Fund Board (NRSFB) which provides project grants for basic, strategic and applied research in universities. The total budget for biotechnology projects in the period 1994 to 1997 was 117 million €.

(3) Managing BioResearch Ireland (BRI).

The bulk of BRI activities take place in five biotechnology research centres established on the campuses of the five leading Irish universities. BRI carries out contract research in each of the fields related to its centres and funds its own research to develop new products and services. BRI's budget in the period 1994 to 1998 was 14.5 million €, the lion's share of EI's biotechnology expenditure.

The other national organisation playing a major role in the funding of biotechnology research is Teagasc, the development agency responsible for agriculture and food research. It supports mainly applied research and transfers new knowledge and technologies to firms and the farming community. Teagasc only funds research at its eight research centres, most of which specialise in particular agricultural products. The main research topics are in the fields of animal and plant biotechnology, with most investigations involving traditional studies of reproduction, breeding, and production, to which it allocated 17.6 million € in the period 1994 to 1998.

Enterprise Ireland and Teagasc encourage public/private collaboration, and involve industry in policy formation.

The Health Research Board is another funder of biotechnology research. In the period 1994 to 1998, it allocated 4.9 million € to biotechnology research in the form of project grants and direct funding for specialist research units. Several other charities and government agencies also allocate small amounts of funds to biotechnology research. The main research areas supported are plant biotechnology, animal biotechnology, cell factories and human and veterinary biotechnology. A review of Irish biotechnology research did not find any research programmes which funded socio-economic or ethical aspects of biotechnology. In 1999, however, an expert panel was established to consult with the Irish public on the risks and benefits of GMOs in the environment.

The total Irish expenditure on biotechnology R&D between 1994 and 1998 was about 46.3 million € (Martin 1999). EI and Teagasc were responsible for 85 % of all biotechnology R&D expenditure, and they allocated the majority of these funds to industrially relevant research (by Enterprise Ireland) or agricultural and food industry relevant research (by Teagasc). Only a very small proportion of funds supported basic research, until the Science Foundation Ireland (SFI) was launched in 2000. It is a competitive research grants scheme and a major task is technology foresight, which led to a significant increase in research funds for basic research. Its fund of 635 million € for the period 2001 to 2006 will focus equally on biotechnology and information and communications technology, with the objective to create a critical mass of world-class research in these two areas. Funds are available for research in areas from curiosity-driven to applicable research and also support campus-industry research partnerships. In 2000 Teagasc also directed more funds to biotechnology. It allocated 32 million € over five years to its research institutes to develop capability in biotech.

The Biotechnology industry in Ireland is supported by a workforce of highly trained scientists. The proportion of Irish people aged 25 to 34 with scientific qualifications is the highest in the OECD countries (OECD internet site) and the number of students in tertiary education in Ireland has increased by 80 % over the last ten years (Canning 2000). The number of graduates from Irish universities conferred with a degree or diploma in a biotechnology-related discipline increased from 505 in 1993 to 682 in 1996. A variety of full-time and part-time biotechnology courses are now available from universities, institutes of technology and colleges throughout Ireland. The continued expansion of the biotechnology industry in Ireland has been assisted by a consistent increase in the number of biotechnology graduates qualifying with a diploma, bachelor's degree, masters degree or a PhD.

This increase was primarily due to the development of new biotechnology courses and the expansion of existing biotechnology courses which were direct results of the demands from the Irish biotechnology industry for higher numbers of graduates trained in the principles of modern biotechnology. National policies support the production of skilled labour. As of now, Ireland annually produces about 500 graduates in biotechnology-specific disciplines and a total of about 2,000 in various biomedical and scientific disciplines who are employable within the biotechnology sector.

Despite the substantial number of students with degrees in biotechnology, the recruitment of new staff is becoming difficult for public research organisations, because a lot of scientists have been leaving the university after their first degrees and taking jobs in industry. Biotechnology firms on the other hand have no problems recruiting researchers with relevant skills. The large firms are able to recruit staff even from overseas. One of the venture capital funds aims to attract highly skilled people from abroad to return to Ireland to establish businesses (Canning 2000).

The new staff are excellent from a technical point of view but need a broader business background and management and analytical skills. In addition, the discipline is changing so rapidly that there are big gaps in certain areas. In biotechnology manufacturing and process development, there is a huge deficit of appropriately trained people. As proposed by the companies, the students doing a science PhD should have special courses in innovation, entrepreneurial research, IPR and competitive intelligence. In reply to this need, BRI is involved in training programmes in business planning and management for researchers and entrepreneurs (Canning 2000).

A7.2.2 Commercialising biotechnology

Technology transfer mechanisms for public sector research are relatively strong in Ireland compared to other European countries. Technology transfer is a central goal of EI's and BRI's work. Technology is transferred to existing firms and new start-up and spin-off companies are created. In the past a significant amount of technology transferred to industry by BRI has gone to foreign firms rather than indigenous enterprises. Against this experience a shift of focus towards the support of start-up firms took place during the last years. Thereby a domestic biotech sector should be supported.

Every university and technical college has an industrial liaison office and EI also runs a Company Campus Programme, designed to assist individuals to commercialise R&D on the college campus. This programme supports the development of existing companies and the establishment of new companies. It provides assistance to researchers interested in commercialising R&D emerging from the college campus. It helps academic entrepreneurs or campus companies to assess the commercial viability of their innovative technology. Support is available in the form of business development advice, financial assistance, mentor facilities and specifically designed part-time business training courses.

Public research organisations and firms that are interested in pursuing patents seem to have access to the professional expertise required. There seems to be good synergy between small firms wanting to exploit the public research organisations' knowledge and public research organisations looking for commercial partners. Regrettably most Industrial Liaison Offices in the university system are overextended and have completely inadequate financial resources for optimal identification, protection and maintenance of intellectual property emanating from within the Universities research departments. The main obstacles for patent applications are political (disagreements between countries), a lack in the training of academic scientists concerning the process of patenting or commercialisation of their results and inadequate financial resources.

The EU Framework Programmes have also played an essential part in fostering university-industry linkages, with increasing numbers of Irish companies becoming project participants. The Irish Innovation Relay Centre is one of a network of 68 Innovation Relay Centres (IRCs) spanning the EU and associated countries. This international network is a source of technology opportunities and the IRC in Ireland assists Irish industry with their individual technological needs. The objective of the Irish Innovation Relay Centre is to help Irish SMEs identify solutions to their technological problems and access European technology by promoting both inward and outward technology transfer.

A7.2.3 Creating a supportive framework for biotechnology

Since 1996, EI has been running a programme to contribute to the costs of developing or expanding campus incubation and R&D facilities at universities. The Intellectual Property Unit of Enterprise Ireland gives advice on the protection, development and commercialisation of inventions that arise from Government sponsored research from universities, industry and private individuals and in certain circumstances will provide funding for patent filing expenses.

Regulation

EC biotechnology regulations have been the basis for Irish regulations since 1994. Ireland has no special orphan drug or fast-track regulation for certain drugs.

IPR

Irish Patent Law (1992) permits membership of International conventions, including the European Patent Convention (EPC) and the Patent Co-operation Treaty (PCT). Most Irish universities have now formulated a college patents policy. Normally, the university will own the technology, and the academic will be listed as an inventor on the patent (as appropriate). The university will be prepared to incur the costs of patent filings if it considers the technology to have some commercial potential. Universities typically set guidelines on the division of income arising from successful exploitation of the patent between the inventor, the college and the faculty or department where the research was performed, with a sliding scale that increases the proportion for the college as income from the patent rises.

The Intellectual Property Unit of Enterprise Ireland gives advice on the protection of inventions and in certain circumstances provides funding for patent filing expenses through its Intellectual Property Assistance Scheme.

Companies can benefit from financial incentives which make patent royalties exempt from tax. The Finance Act 1973 allows income from a qualifying patent to be disregarded for tax purposes and patent royalty tax exemptions are routinely exploited by the larger biotechnology companies in Ireland.

Financing

Fiscal policies, especially low corporation tax for companies, tax exemption for income from patents are important measures to support commercial development. The Business Expansion Scheme of EI is another helpful instrument for firms to raise finance (e. g. to obtain investment from business angels). When a company invests in expansion, the scheme provides matching funds (half as a grant and half as preferential shares). EI also provides investment funds for start-up companies. In terms of new high-tech company formation several support schemes are available, notably the Campus Companies Programme. Several companies used government grants as a form of investment. However, these grants require companies to claim reimbursement of costs after they have been spent. An advance would be more appropriate for new firms who may lack funds.

There is limited availability of venture capital. A set of initiatives were put in place during 1994 to 1999 to address the shortage of venture capital for biotechnology firms. However, the biotechnology industry in Ireland did not benefit to any great extent, with the exception of the Campus Companies Venture Capital fund and the Millennium Entrepreneur Fund. General interest in the promise of biotechnology amongst the international venture capital community did not translate into investment by Irish venture capital in this sector in Ireland. There are several reasons why Irish venture capitalists are reluctant to invest in biotechnology: the perception of biotechnology as "risky", the early stage in the life cycle of the sector in Ireland and the perceived contrast in complexity of biotechnology start-up companies against a background of very successful Irish Information Technology (IT)-based start-ups. In 2002, Enterprise Ireland began to address the special needs of the biotechnology sector in the form of a dedicated seed-fund. It involves a partnership with financial institutions in order to share the risks.

Ireland has effectively deployed consistent tax and financial incentives to attract inward foreign investment, particularly US firms setting up European bases. Many studies have examined the impact of Foreign Direct Investment (FDI) on the Irish economy. Several have highlighted the ambiguities associated with defining Ireland as a successful example of industrialisation through FDI (O'Malley 1985). It is argued that this high technology sector has been "imported" using FDI policies (Kerr 1996), with a clear division in terms of ownership between the high technology, mainly foreign owned companies and the lower technology indigenous companies. The tendency to rely on head office for strategic functions has meant that in skilled employment terms and R&D terms their contribution has been lower than in comparative firms in other countries (Foley 1991; Foley & Griffith 1991, 1994; Foley & McAleese 1991, 1994; Cooper and Whelan 1973). Also, the belief that foreign high technology industries would act as a stimulus to indigenous services and supply companies has not been realised to the extent that was expected (O'Huallachain 1984), although this situation has ameliorated in recent years.

Socio-economic issues

It was not until the 1990's that science topics, specifically the role of modern biotechnology in food and agriculture and the concomitant consequences to the environment, began to appear on a regular basis in the national media (Barbagallo & Trench 1999; Kirby 1999). According to Eurobarometer and other public opinion polls, the awareness of biotechnology was relatively low in Ireland, but a high proportion of the interviewees found the genetic engineering of crop plants acceptable. Later Eurobarometer surveys established a continuing low knowledge but raising concern about the security of GM food and animal cloning.

In 1999, the Government issued several initiatives to raise the public awareness of S&T in general. In addition, a public consultation process was set up to facilitate public input into the formulation of its policy in relation to GMOs and the environment (Dempsey 1999). Despite this, public knowledge of modern biotechnology remained poor.

A7.3 Assessment of biotechnology performance

The performance of the biotechnology innovation system in Ireland is analysed with the help of some defined indicators which cover the entire innovation process from scientific research to introduction of products in the market.

A7.3.1 Performance related to scientific activities

The scientific performance is measured by bibliometric indicators. For 1990 to 1995, in the field of biotechnology, 409 publications with Irish authors can be found, the number increased to 1,103 publications between 1996 and 2001. Relative to the population size, the number of publications increased from 115 per million inhabitants between 1990 and 1995 to 298 per million between 1996 and 2001. For the same periods, in the EU the numbers increased from 136 per million to 318 per million indicating that Ireland managed to slightly reduce its under-performance. With respect to publishing intensities related to the total number of researchers, Ireland outperformed the EU with 150 biotechnology publications per thousand researchers[58] in the last five years compared to only 137 in the EU. In the period from 1990 to 1995, the Irish publication activity in biotechnology had accurately been on the same level with the whole EU (65 publications per thousand researchers both).

As figure A7.1 shows, the percentage of biotechnology publications of all Irish publications increased approximately linearly from 1991 on with a slight superiority to the EU in the last two years. This indicates a relatively high relevance of biotechnology research in Ireland.

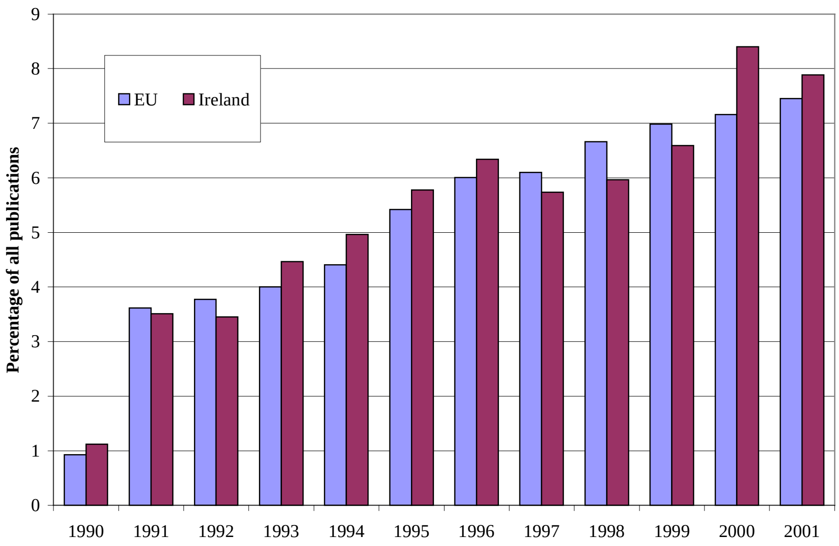
---

58 Researchers in total, not restricted to those working in biotechnology.

The specialisation profile within biotechnology research is given by figure A7.2, which shows the distribution of biotechnology publications in seven subfields. As indicated by the number of publications, animal biotechnology, to a smaller extent also platform technologies and bioprocessing attract special attention in Ireland compared to the EU, whereas diagnostics and therapeutics, plant biotechnology and cell factory are underrepresented in Ireland.

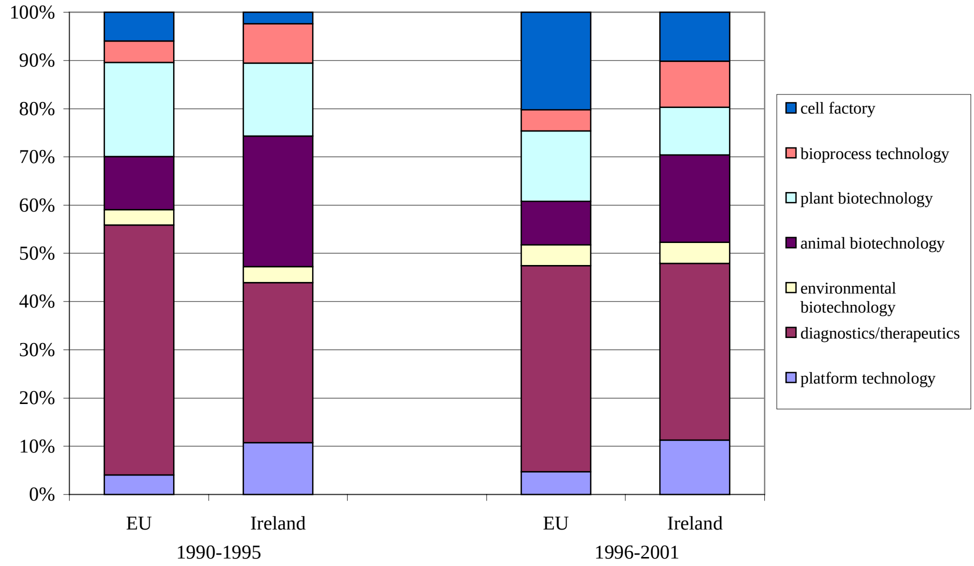
In summary, the bibliometric analyses show a large increase of scientific activities in Irish biotechnology in the last years. Ireland was able to reduce its under-performance relative to the EU. Biotechnology research is of high relevance in Ireland, especially animal biotechnology, but also platform technologies and bioprocessing.

Figure A7.1: Share of publications in the field of biotechnology of all publications in Ireland



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

Figure A7.2: Share of different fields in biotechnology in the EU and Ireland[59]



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

A7.3.2 Performance related to commercialisation

Biotechnology companies

The biotechnology industry in Ireland can be subdivided into two specific groups. The first group includes biotechnology companies that are subsidiaries of multinational companies, which generally perform product R&D on a relatively small scale in Ireland and use their facilities in Ireland predominantly to manufacture biotechnology products. The second group of companies in the Irish biotechnology industry is comprised of indigenous Irish biotechnology companies. They have focused upon developing diagnostic products for the healthcare market. Indigenous Irish biotechnology companies maintain significant R&D programmes in their own laboratories as well as in association with collaborating laboratories in Irish Universities. These companies often also manufacture their products by themselves.

In 2000, 31 companies (public and private) were active in the field of biotechnology in Ireland. Between 1996 and 1999, the number had constantly increased from 26 to 43 firms with the highest leap in 1997, a development which was totally in accor-

59 In the data for the category "cell factory" an unexpectedly high increase is found between 1994 and 1995 over all countries. This might result from changes in the documentation practice and explains in part the differences between the two periods of time in figure A7.2 for "cell factory".

dance to the whole EU. With around 75 % Ireland has a relatively high proportion of small companies (with 1 up to 20 employees), the other firms have more than 50 employees (OECD, data from 2000).

Venture capital invested in biotechnology

Table A7.1 shows the amount of venture capital that has been invested in Irish biotechnology between 1990 and 1995 as well as between 1996 and 2000. In the latter period around 7.2 million € venture capital has been invested in biotechnology companies. In absolute figures the amount has increased nearly five times, and also in relation to the biotechnology venture capital in the whole EU a slight increase can be found.

Table A7.1: Venture capital invested in biotechnology

Year	**absolute value**		**% of venture capital invested in EU**
	in 1,000 €	in 1,000 PPP[60]	
1990 to 1995	1477.70	1658.689	0.38
1996 to 2000	7193.45	7695.152	0.43

Source: EVCA

As table A7.2 indicates, the amount of biotechnology venture capital increased not only in absolute figures, but also relative to the mean population nearly fivefold in Ireland but has not yet reached the EU level.

Table A7.2: Indices of venture capital invested in IE

	Ireland		**EU**	
Year	**absolute amount**	**amount relative to mean population**	**absolute amount**	**amount relative to mean population**
	in 1,000 PPP	in PPP per inhabitant	in 1,000 PPP	in PPP per inhabitant
1990 to 1995	1658.689	0.466	438919.599	1.191
1996 to 2000	7695.152	2.109	1783683.684	4.760

Source: EVCA

60 PPP: purchase power parity

However, this positive trend in Ireland should not be overestimated, because it mainly relies on an extraordinary high level of investment in the year 1996, from which on the amount of venture capital decreased dramatically.

Patent applications

Between 1990 and 1995, Irish actors applied for 34 patents for biotechnological inventions (9.6 per million inhabitants and 5.4 per thousand researchers, respectively), from 1996 to 2000 for 79 patents[61] (21.3 per million inhabitants and 10.7 per thousand researchers, respectively). In comparison to the figures for the whole EU this shows the success of the policies to strengthen the Irish biotechnology innovation system: Between 1990 and 1995, the EU had 16.2 patent applications per million capita or 7.8 per thousand researchers, clearly more than Ireland. For the following five years, with 25.3 patent applications per million inhabitants, the EU had only a small advantage left. But relative to the number of researchers Ireland has totally caught up with the EU (10.9 patent applications per thousand researchers).

The ratio of biotechnology patents to all Irish patents was 6.3 % between 1990 and 1995 and increased to 8.6 % in the following five years. The values for the EU were 3.4 % and 4.5 %, respectively, what indicates a relatively high relevance of biotechnology inventions in Ireland. By far most of the patents came from the subfields of platform technologies and diagnostics/therapeutics, in recent years also from bioprocessing technologies and cell factory.

Other indicators

There was just one initial public offering (IPO) of a biotechnology company in Ireland between 1995 and 2000: Axogen went public in 1996[62].

According to data from EMEA no bio-medicines originating from Irish companies were approved by EMEA between 1995 and 2001.

Four field trials of GM plants were notified to the EU, two in 1996 and two in 1998, all of them for sugar beet varieties. The Irish notifications were carried out by large firms and account for 0.2 % of all field trials in the EU.

In summary, the commercialisation indicators underline the rather early stage of the Irish biotechnology industry. However, in recent years a considerable growth of

---

61 The patent numbers for the year 2000 are estimated.

62 Sources: E&Y Annual European Life Sciences Reports, websites by Nasdaq, Neuer Markt, London Stock Exchange, Euronext

start-up companies can be observed which not least has benefited from an increasing support of start-up formation by Irish biotechnology policy. The early stage of the industry is directly related to the problem of acquiring venture capital, because many venture capital firms have not yet acknowledged the prospects of this young sector in Ireland and it is still difficult for these firms to meet the requirements of venture capitalists. On the other hand some public initiatives trying to draw venture capital into this sector seem to show some first positive results. In general, the prospects of commercial biotechnology in Ireland are rather positive also because Ireland provides an entry market for foreign firms to the European Union.

A7.4 Conclusions

The main policy goals concerning Irish biotechnology was to commercialisation. As the performance indicators show, related policies seem to have been quite successful after a certain learning phase in the early 1990s where know-how and technology were transferred mainly to foreign firms. In consequence, a stronger focus was put on building up an own bioindustry by installing various mechanisms to support start-ups.

The national Biotechnology Programme, BioResearch Ireland, as part of Enterprise Ireland, comprises research funding as well as support for technology transfer, support with commercialising R&D and for setting up start-up companies. In co-operation with the universities, patent applications are supported by special counselling as well as financial aid, but most Industrial Liaison Offices in the universities have too scarce financial resources for optimal identification, protection and maintenance of intellectual property emanating from within the Universities research departments. Despite this, in general the co-operation between small firms and public research organisations seems to work well. Setting up campus incubators proved to be another effective instrument for commercialisation.

To finance these measures, Ireland effectively deployed EU structural and cohesion funds. Fiscal policies, especially low corporation tax for companies and tax exemption for income from patents are important measures to support commercial development. Besides the establishment of SMEs, this supportive climate attracted foreign large firms which mainly established production facilities in Ireland. Despite the fact that not much research was financed by these firms in Ireland, the attraction of foreign firms offered job opportunities to biotechnology staff. The Irish education system flexibly reacted to these needs by establishing university courses and programmes for the respective disciplines, so that Ireland now has a highly qualified workforce in this field.

A problem was and still is the low amount of venture capital despite several initiatives to ameliorate this situation. A main reason might be the early stage in the life cycle of the sector in Ireland. In 2002 a dedicated seed-fund was introduced with financial institutions in order to share the risks. Another problem is the "small country problem", meaning that it is necessary to look abroad for getting access to specific knowledge and technology. Support for international networking would help to solve this problem.

In research, Ireland concentrated on applied research, only in the last few years a need for more basic research was recognised in the context of the national foresight process and more funds were directed to basic research.

A8 Biotechnology innovation system in United Kingdom

A8.1 Introduction

The UK has a population of 59.8 million (year 2000) and its gross domestic product (GDP) amounts to 1,524,416 million PPP (year 2001). It is a heavily industrialised country with an economy based on service, trade and manufacturing. Biotechnology and the pharmaceutical industry play an important role in the UK economy. With Glaxo SmithKline and Astra-Zeneca two of the largest pharmaceutical companies of the world are located in the UK. During the 1990s the UK has been the leading country in the commercial development of biotechnology in Europe.

The gross domestic expenditure on R&D (GERD) summed up to 27,094.3 million PPP in 2000 (OECD 2002). This corresponds to a ratio of 1.86 % GDP which is slightly below the EU average of 1.88 % and also below the OECD average of 2.24 %. Since 1996 the GERD share in the GDP remained approximately constant in the UK. However, while the UK has been above the European average throughout most of the 1990s, it fell below the European average since 1998. GERD per capita population was 453.4 PPP in the year 2000 which is very close to the European average of 457.7 PPP in the same year. Since 1996 per capita GERD increased continuously in the UK at a similar speed as the GDP. 48.5 % of GERD was financed by industry in the year 2000 compared to 55.5 % for the European Union and 62.9 % for the OECD. Obviously industry contribution to R&D financing in the UK is lower compared to other industrialised countries. However, since 1998 there is a trend of increasing industry contribution to GERD resulting in a share of 49.3 % in the year 2000. The total number of researchers was 157,662 (full time equivalent (FTE)) in 1998. This corresponds to a ratio of 5.5 % per thousand total employment which is slightly above the European value of 5.4 % and below the OECD ratio of 6.4 % in the same year. Taken together, these indicators show that in terms of input to R&D the UK ranks roughly at the European average.

In the following the biotechnology innovation system of the UK will be characterised along different dimensions: in a first step (see A8.2) the policy framework supporting biotechnology in the UK will be described. In A8.3 the performance of the UK biotechnology innovation system will be assessed and in the final A8.4 conclusions will be elaborated with a focus on the effects of different policies. The main question will be how different policy instruments contributed to shaping the present situation of the UK biotechnology innovation systems.

A8.2 Policy framework

A8.2.1 Creating and sustaining a biotechnology knowledge base

Policies for supporting biotechnology in the UK emerged already in the early 1980s. Strengthening the science base and stimulating the commercial exploitation of biotechnology research have been two of the main policy goals until today. The funding system for biotechnology research in the UK can be characterised as a pluralistic system with 17 different government organisations and several charities providing funds (Martin 1999). The most important organisation supporting biotechnology is the Biotechnology and Biological Science Research Council (BBSRC) under the Office of Science and Technology (OST) which provides more than 50 % of all funding. Other important organisations include the Medical Research Council (MRC), the Ministry of Agriculture, Fishery and Food (MAFF, now Department for Environment, Food and Rural Affairs (DEFRA)) and the Welcome Trust. The latter is the largest medical research charity in the world and plays a very important role in the British funding system. For example, the trust invested heavily in the sequencing of the human genome and helped to establish the Welcome Trust Genome Campus near Cambridge where some of the world's largest sequencing efforts are taking place.

The total budget for biotechnology research 1994 to 1998 amounted to 2,572 million € (Martin 1999). About 17 % of these funds were provided by charities, the remaining 83 % by government funding. About half of the government funding can be characterised as non-directed support for basic research. This means that funds were allocated by research councils to universities in the form of response mode grants. A little more than 50 % of government funds during 1994 to 1998 were directed specifically towards biotechnology via programmes supporting basic research in universities, funding of research institutes and research training. The main instruments for supporting basic research in universities by the research councils are grants which are allocated on the basis of competitive peer review. They are given not only for basic research but also for strategic (directed) research and to some extent for funding longer-term research in different research units. As a guidance for the direction, balance and content of research council's funding activities the UK technology foresight programme, which was launched in 1994 by the Office of Science and Technology, is used.

In addition to supporting mainly technical areas of biotechnology, there is also some funding for socio-economic research which is provided mainly by the Economic and Social Research Council and the Nuffield Foundation. Funds are used for projects on ethical, legal and social aspects of biotechnology as well as activities aiming at increasing public understanding of science.

A8.2.2 Commercialising biotechnology

Policies to support the commercialisation of biotechnology in the UK seem to be based on the believe that maintaining and expanding a strong science base is the best vehicle to achieve commercialisation (Senker et al. 2000). In consequence, there is only scarce direct funding of industry and only few initiatives aim at building up technological capabilities for the industry. Measures in this category include the SMART Programme run by the DTI which provides awards to small and medium-sized enterprises on a competitive basis to help them develop innovative ideas. This measure should help small firms to reach a stage to be able to attract investment finance. Awards are given to the costs for feasibility studies and for developing innovative products or processes. The Manufacturing for Biotechnology Programme of the DTI helps companies to find the research and technical production capabilities which are needed for producing biotechnology products. This is achieved by organising workshops and seminars on manufacturing in biotechnology and providing training grants for small and medium-sized enterprises.

A number of instruments aims at encouraging the commercialisation of biotechnology from public sector research organisations including support for firm creation:

The MRC's collaborative centres provide an environment for academic and industry researchers to work together, and also serve as incubator facilities. The MRC seeks to create spin-off firms from the work in these centres. In addition to these central initiatives also regional government agencies in Scotland have set up Technology Ventures to create spin-out firms. There are many science parks in or near university campuses. However, these have grown up at the initiative of universities rather than through any government scheme (Gristock & Senker 1999). In 1999 the Science Enterprise Challenge was launched, providing finance for eight enterprise centres in universities. The centres teach entrepreneurship and business skills in the science and engineering curricula, and also commercialise research (Gristock & Senker 1999). From 1999, the Higher Education Reach Out to Industry and the Community programme provides additional core funding to universities, to support relationships between higher education and industry and to improve technology transfer.

Another generic instrument to support technology transfer from public sector research organisations is the Teaching Company Scheme which provides funds for placing graduates in a company to work on a specific project supervised by academic and industrial researchers. Finally, most of the universities have technology transfer officers to promote co-operation with industry and business link offices which are supported by the DTI which aim at providing companies with various business support services (Gristock and Senker 1999).

The most important instruments to encourage the commercialisation of biotechnology research in the UK comprise initiatives supporting the collaboration between public sector research organisations and industry. The government's main mechanism for supporting collaborative research between industry and public sector research organisations is the LINK Programme. It is a generic programme not specific for biotechnology. However, it includes several biotechnology-related subprogrammes which receive about 2 % of the total LINK funding for directed research (Martin 1999). Public bodies provide up to 50 % of the costs of a collaborative project, requiring that the balance is provided by industry. Participants in link projects have formal agreements on technology transfer and about intellectual property and the DTI receives royalities if marketable products are generated from the research within five years.

In addition to the LINK scheme there are other incentives for academic scientist to enter into collaborations with industry. These include the ROPA Awards which are granted to academic scientists who receive substantial funding from the private sector and can be used for curiosity-driven research in new areas as selected by the scientist. The Joint Research Equipment Initiative provides funds for equipment needed in high-quality research areas and is eligible to academic scientist who had been able to acquire industrial or other external funding.

In order to increase the adoption of biotechnology by traditional industrial sectors, the DTI launched the Biotechnology Means Business Initiative in 1994. This initiative comprises a whole set of measures to help companies independent on their size and industrial sector to explore and exploit biotechnology. These include telephone helplines, seminars and workshops, literature on case studies, fact files and question- and answer-booklets. In the course of this programme it was realised that raising awareness of different industries alone was not sufficient. Rather it turned out to be important to encourage domestic biotechnology supply industries to provide the technology which may be demanded by the target industries. Therefore, the follow-up programme BIO-WISE launched in 1999 not only gives advice to traditional industries on how to use biotechnology, but also supports the development of the biotechnology supplier industry in the UK. It provides the following services: independent advice through a helpline and website, free publications describing benefits of using biotechnology, free visit to SME from an industrial biotechnology specialist, grant support to companies to demonstrate the benefits of biotechnology, information and advice to biotechnology suppliers and free events that present biotechnology in action and provide opportunities for networking.

A8.2.3 Creating a supportive framework for biotechnology

Regulations general

Biotechnology-related regulations within the UK conform to EC Directives. A number of regulatory and technical bodies provide advice to government. There has been no special orphan drug law in the UK but European Orphan Drug legislation became law in April 2000. In 1999, the Government set up strategic advisory bodies to advise on how developments in biotechnology may require changes to regulatory committees, procedures and guidelines (Senker et al. 2000).

Intellectual property rights

Two different systems govern patenting in the UK: the national system according to the Patents Act 1977 and the European patent system governed by the European Patent Convention from 1978. European patent applications can be filed at the European Patent Office (EPO), for national applications the UK Patent Office is the responsible authority. Since EPO applications are finally also converted into national patents, they are also governed by the corresponding national laws. Therefore, although the application procedures are dealt with by different authorities (either EPO or National Office), most of the legal procedures and interpretations are handled at national courts of each country for which patents have been granted. Important differences between national and European patents are the costs which for European patents are rather high, in particular for small and medium-sized enterprises. This is mainly due to the required translations into the national language of each contracting state. Concerning ownership of intellectual property there are differences in the UK depending on the agency funding the related research (Senker et al. 2000). The MRC owns and exploits the results of all the work it funds. It has a technology transfer group which manages its own patents and actively licenses them out. DEFRA owns the IP from the work it funds, but splits royalties with the investigator. The BBSRC considers that IP is owned by the institution in which the research is carried out, but provides advice on intellectual property and encourages its exploitation by the investigators and institutes it funds. The main patenting problem for SMEs in the UK are differences between the US and European systems.

Financing

During the 1990s the UK has been one of the best places in Europe for obtaining private equity. Equity is provided mainly by institutional investors from the private and public sectors. UK-based funds are attractive to institutional investors because they are made tax effective by the respective legal framework (Senker et al. 2000). Venture capital investments in the UK have concentrated on the later development stages, so that there is a lack of venture capital for the more risky early seed and start-up stages of company development. Despite these problems there are only few policy measures aiming at further improving or facilitating venture capital availability for biotechnology. These initiatives include the Biotechnology Finance Advisory Service which was set up by the DTI in 1995 as a small pilot programme to improve awareness of and access to sources of finance for existing biotech firms and new start-ups. In addition, the MRC has set up an investment fund for financing start-up companies in the biotech and health care sector. University Challenge, launched in 1998, provides competitive seed funds for universities to transfer research into potential new businesses.

Other measures which contributed to improving the availability of finance for biotech firms are the criteria for listing on the London Stock Exchange being relaxed in 2001. While formally companies had to have two products in clinical trials, they can now apply just showing promising R&D activities (Ernst & Young 2001). Biotechnology companies were also helped by the announcement in 2000 of tax relief for industrial SMEs carrying out R&D and for firms involved in corporate venturing (Trendchart).

Socio-economic issues

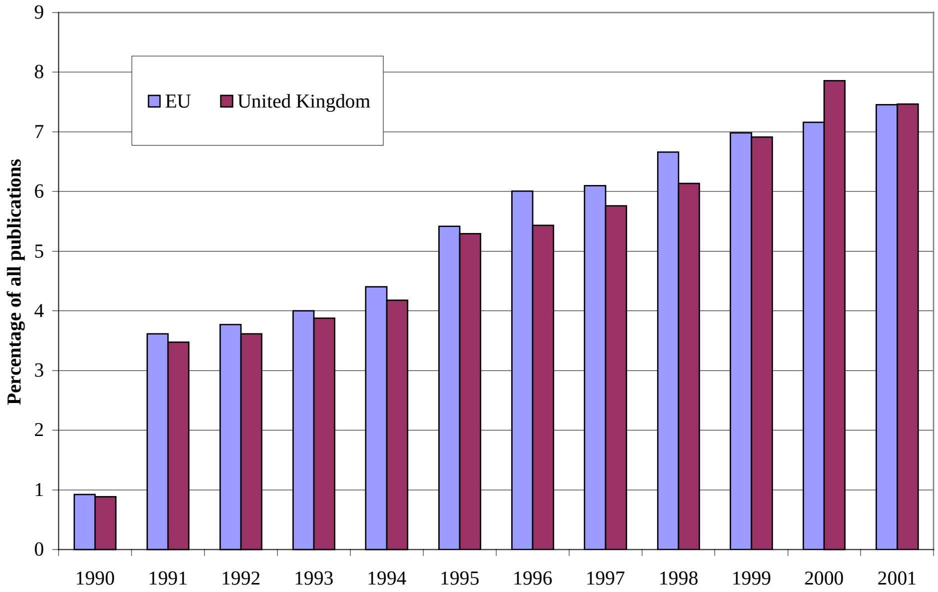
The Economic and Social Research Council has supported a small number of projects on ethical, legal and social aspects of biotechnology. In addition, the BBSRC funds activities to increase public understanding of science, in particular related to the release of GMOs. It has also established an advisory group to provide guidance about public perceptions of social and ethical issues arising from the research it funds. The MRC provides some support for the work carried out by the Nuffield Council on Bio-Ethics.

A8.3 Performance of the UK biotechnology innovation system

A8.3.1 Performances related to scientific activities

Publication activities in the UK in biotechnology increased considerably during the 1990s. While the total number of biotechnology publications summed up to 12,126 in the period 1990 to 1995 this number more than doubled to 28,368 publications in the period 1996 to 2001. A very significant increase of publication output in biotechnology is also obvious if we relate publications to the size of the country. In the first period (1990 to 1995) 209 publications per million capita were made in the UK, in the second period (1996 to 2001) publishing intensity increased to 479 publications per million capita. Compared to the European average (136 publications per million capita in the first period and 318 publications per million capita in the second period), the UK biotechnology system performs well above the average. In order to get an indication of the efficiency of the research system, publication output is also related to the number of researchers[63]. In the first period publication intensity related to the number of researchers amounted to 89 per thousand researchers, which was above the European average of 65 publications per thousand researchers. In the second period publication intensity increased substantially to 190 publications per thousand researchers, compared to an EU level of 137 publications per thousand researchers. Taken together, publication indicators point to a good performance of the UK biotechnology innovation system, in particular the publication intensities are clearly above the European average, indicating a good efficiency of the British system with respect to publication output.

Figure A8.1: Share of publications in the field of biotechnology of all publications in the UK



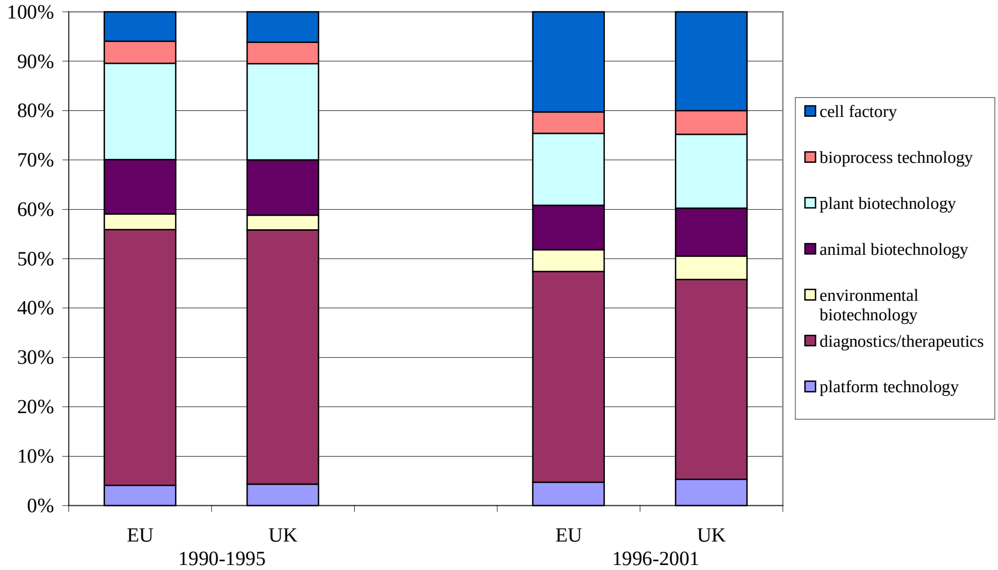
Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

In order to assess the significance of biotechnology in the UK research system, we analysed the share of biotechnology publications in all publications. While in the year 1990 less than 1 % of all publications were in the field of biotechnology, this ratio increased considerably to 8.7 % in the year 2001. Obviously, biotechnology gained importance among the various research activities in the UK. However, if we compare the UK with the European situation (figure A8.1), it becomes obvious that the increasing importance of biotechnology is not a specific UK phenomenon but took place all over Europe. The situation in the UK developed more or less in line with the European average.

63 Since official data on the number of researcher in biotechnology are not available, we use the OECD figures for all researchers (full time equivalents) in the country.

The specialisation profile of the UK compared to the European situation as a whole is presented in figure A8.2. Not surprisingly there are no pronounced differences between the UK and the European profiles, which is due to the fact that the UK is contributing roughly a quarter of all European publications. The major changes in the profile relate to the areas cell factory and environmental biotechnology which increased their shares in the UK as well as in Europe at the expense of all other areas.

Figure A8.2: Share of different biotechnological fields in biotechnology in UK and the EU



Source: Fraunhofer ISI 2002, data: Science Citation Index via STN

A8.3.2 Performance related to commercialisation

Biotechnology firms

The UK was one of the first European countries to develop a strong biotechnology industry. The increase of the number of biotechnology firms in the UK is summarised in table A8.1. Roughly 75 % of the firms have less than 50 employees. The focus of activities of the UK biotech industry is pharmaceuticals and also equipment and supplies for biotechnology. There are only few firms concentrating their activities on the agro-food sector (Senker et al. 2000).

Table A8.1: Number of biotechnological firms in UK

	1996	1997	1998	1999	2000
Number of bt firms	180	248	265	274	275

Source: Ernst & Young

Venture capital invested in biotechnology

The UK has one of the most favourable legal and fiscal environments for private equity in Europe with the Alternative Investment Market and other stock exchanges providing the equity firms with a number of exit opportunities (see chapter 4.5.2). Accordingly, the amount of venture capital invested in UK biotechnology increased sizeably during the 1990s. Between 1996 and 2000 about 392.4 million € of venture capital were invested in UK biotechnology firms (table A8.2). This corresponds to a threefold increase compared to the first half of the 1990s. As indicated in table A8.3 venture capital investment in biotechnology in the UK also increased in relative terms. In addition, the growth is well above the European level. However, during the 1990s a number of other European countries was able to attract more venture capital for biotechnology. In consequence, the share of the UK venture capital investments in biotechnology in Europe dropped from 34 % in the first period to 21 % in the second period. Despite this relative decrease, the data on venture capital investment in biotechnology confirm that venture capital firms perceived the UK as a preferred place in Europe for industrial development of biotechnology.

Table A8.2: Venture capital invested in UK biotechnology

Year	**absolute value**		**% of venture capital invested in EU**
	in 1,000 €	in 1,000 PPP[64]	
1990 to 1995	135842.84	149223.471	34.00
1996 to 2000	392350.54	383002.714	21.47

Source: EVCA

64 PPP: purchase power parity

Table A8.3: Indices of venture capital invested in UK

	UK		EU	
Year	**absolute amount**	**amount relative to mean population**	**absolute amount**	**amount relative to mean population**
	in 1,000 PPP	in PPP per inhabitant	in 1,000 PPP	in PPP per inhabitant
1990 to 1995	149223.471	2.570	438919.599	1.191
1996 to 2000	383002.714	6,.488	1783683.684	4.760

Source: EVCA

Initial public offerings

The UK is the country in Europe with most initial public offerings (IPO) in biotechnology. Between 1995 and 2000 all in all 31 biotechnological Firms went public. Table A8.4 shows the number of IPOs by year.

Table A8.4: Number of initial public offerings (IPO) of UK biotech firms between 1995 and 2000

	1995	**1996**	**1997**	**1998**	**1999**	**2000**
Number of IPO	4	8	4	5	0	10

The five first UK biotech companies which went public were: Peptide Therapeutics; Biocompatibles International; Polymasc Pharmaceuticals; Stanford Rook. These companies were followed by Vanguard Medica; PPL Therapeutics; Therapeutics Antibodies; Shire Pharmaceutical; Phytopharm; Oxford Biomedica; Alizyme; Chemical Design in 1996. In 1997 Galen Holdings; Cambridge Antibody Technology; PowderJect Pharmaceuticals; Core Group went public. One year later the IPO of Quadrant; Oxford Asymmetry; Oxford GlycoSciences; Bioglan; Antisoma took place. The year 2000 was the year with most IPO. Ten biotech firms went public in this year: Gemini Genomics; Weston Medical; Pharmagene; Genetix Group; Profile Therapeutics; GeneMedix; ReNeuron; BioFocus; ReGen Therapeutics; Fulcrum Pharma.

Drugs approved

Altogether nine biomedical drugs developed in the UK were approved by the EMEA between 1995 and 2001: in 1996 and 1997 two approvals each, in 1999 one approval, in 2000 three and in 2001 one. The UK share of approved drugs in whole Europe comes to 21 %.

Field trials of GMO plants

209 field trials of GM plants were notified to the EU. Table A8.5 shows the number of approved notifications per year. Since the middle of the 1990s field trial notifications became stagnant and dropped to a rather low level by the year 2001.

Table A8.5: Approved notifications of field trials with GMOs in UK per year

	1991	**1992**	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**
approved notifications	7	7	12	23	38	22	27	22	11	23	10

Source: IHCP 2002

The field trials were notified for the following plants: oilseed rape (102), potato (35), sugar beet (33), fodder beet (8), maize (7), wheat (7), tobacco (6), chicory (4), two field trials each for barley, eucalyptus and poplar and one field trial each for apple, strawberry and tomato. The UK notifications were carried out by large companies (147), public research (23), universities (21), co-operatives (19), SME (15) and other notifier (5) and account for 12.4 % of all field trials in the EU.

Patent applications

Between 1990 and 1995 the UK filed 1,352 biotechnology patent applications at the European Patent Office. This number increased considerably to 1,915 patent applications for the period 1996 to 2000. Patenting intensity related to population increased from 23 biotechnology patents per million inhabitants in the first period to 32 patents per million inhabitants in the second period. Both values are well above the European average 16 (first period) and 25 (second period) patent applications per million inhabitants. Patenting intensities related to researchers also increase from 10 biotechnology patent applications per thousand researchers in the first period to 13 patent applications per thousand researchers in the second period. Again, both values are above the European average of 8 (first period) and 11 patent applications per thousand researchers (second period). This indices indicate a rather high propensity of UK researchers to patent their biotechnology inventions.

The significance of biotechnology in terms of patenting also increased in the UK during the 1990s. While in the first period 5.9 % of all UK patents were in the area of biotechnology, this ratio increased to 7.8 % in the second period. Compared to the European situation with a biotechnology share of 3.4 % (first period) and 4.5 % (second period) biotechnology has a much higher weight in the patenting activities of the British system.

A8.4 Conclusions

The UK is a leading country of European biotechnology. In particular with respect to the commercial development of biotechnology the UK belongs to the most advanced nations in Europe. The British biotechnology industry can build on a traditionally strong science base which certainly played a crucial role in the early development of the industry. During the 1990s public policy put increasing emphasis on supporting the commercialisation of biotechnology research. The good performance of the British biotechnology industry seems to indicate that these policies have been effective. The British government has developed a whole set of different instruments aiming at supporting commercialisation of biotechnology. The most effective of these instruments in terms of supporting commercialisation seem to be the following:

- Instruments supporting collaboration between universities or public sector research organisations and industry. Most biotechnology firms in the UK are somehow involved in collaborative research with public sector research institutions/universities. The most prominent programme supporting such collaborations is the LINK scheme, even though the administrative efforts needed to get LINK support seem to be rather high. In addition, incentives such as the ROPA scheme and the Joint Research Equipment Initiative encouraged academic scientists to enter collaborations with industry.
- A second set of initiatives aims at improving technology transfer from universities and public sector research organisations to industry. These include initiatives of the research councils to support spin-off companies as well as support for providing information for potential entrepreneurs. The Science Enterprise Challenge can be mentioned as an example for the latter type of initiatives. In addition, the Higher Education Reach Out to Industry and the Community Programme provide funds to university for improving university-industry relations.
- Another set of initiatives is targeted on improving the penetration of biotechnology into traditional industrial sectors in the UK. Such initiatives can be considered as an important way to stabilise biotechnology by creating mutual benefits for biotechnology firms on the one hand (creating new markets), and firms from traditional industries on the other hand (improving competitiveness by using new biotechnology methods). The main instruments serving that purpose were the Biotechnology Means Business Programme and its follow-up BIO-WISE. In this context it is important to mention that the presence of strong science-based large firms in the pharmaceutical and chemical sector in the UK also contributed substantially to the development of the biotech industry. They not only helped to convince the government of the importance of supporting biotechnology, but also provided a potential market for biotechnology firms providing specific services.

In addition to these direct instruments aiming at improving commercialisation of biotechnology in the UK, more indirect measures which tried to enhance the conditions for private financing played a very important role during the 1990s. The most important measures in this context are the relaxation of criteria for listing at the stock exchange markets, tax credits for institutional investors in venture capital funds, and R&D tax credits for firms.

While policies to support commercialisation of biotechnology in general can be considered as successful in the UK, there are some concerns emerging on the future of the biotechnology-related science base. A critical problem in this context is the ability of public sector research organisations to hire skilled staff due to low salaries in the public sphere.

A9 Biotechnology innovation system in USA

A9.1 Introduction

Starting from an already very advanced level, the biotechnology sector in the United States continued to grow dynamically during the 1990s. Growth is driven by a strong science base as indicated for example by selected performance indicators (source: Fraunhofer ISI 2002): Publishing intensity in biotechnology increased from 204 publications per million capita for the period 1990 to 1995 to 449 publications per million capita during the period 1996 to 2001, which is well above the European values of 136 and 317, respectively. During this period the significance of biotechnology publications in all publications also increased from 3.2 % to 8.1 % in the USA. Application-oriented research and experimental development in biotechnology as indicated by patenting intensities present an even stronger dynamics: While during the first half of the 1990s 31.6 biotechnology patents per million capita were applied for by the USA, this intensity increased to 48.9 during the second half, an intensity which is far ahead of the European average of 25.3. The United States is a world leader in researching, designing and producing biotechnology products through the application of various technologies in areas as diverse as agricultural chemicals, pharmaceuticals and medical procedures. As a nature of this sector interactions among different industries as well as between researchers and practitioners are essential for development and progress.

Government policy plays an important role in the biotechnology industry. Support for basic and applied research provides much of the knowledge on which new products are based.

Furthermore, intellectual property on drugs, diagnostic products or gene sequences is a defining feature of the biotech industry. Therefore the country's patent policy, set by Congress and administered by the U.S. Patent and Trademark Office has great influence on the development in biotechnology. The Food and Drug Administration has importance in the commercialisation stage of biotechnology products as they have to approve products with respect to safety and efficacy before they are offered for sale, and they regulate conditions for manufacturing pharmaceuticals and for advertising them to consumers (Cortright and Mayer 2002).

The biotechnology industry is not spread evenly throughout the United States but is concentrated in selected areas, particularly in major urbanised regions on both coasts. With respect to the growing importance of the biotechnology sector, states and regions are developing initiatives designed to foster an environment in which biotechnology companies can succeed and grow. Initiatives address specific needs of biotechnology companies (Battelle Memorial Institute 2001):

- Strong academic research institutions conduction basic research in the biosciences
- Access to early-stage capital
- Transfer of government-funded basic research for product commercialisation
- Specialised facilities including wet laboratory space and specialised equipment
- Highly skilled workforce
- Stable and supportive public policy structure

A9.2 Policy framework

A9.2.1 Creating and sustaining a biotechnology knowledge base

Many technology fields owe their start to breakthroughs in basic research, but a distinguishing feature of biosciences is that biotechnology industry depends on public science much more heavily than other industries and will need a continuing strong linkage between basic research and industry development. Studies furthermore substantiate a positive relationship between R&D intensity and the amount of entrepreneurial wealth created by a high-technology venture (Deeds 2001). Beside the choice of geographic location and management skills scientific knowledge is regarded as one key determinant for successful product development (Deeds et al. 1999).

Support for biotechnology research is extremely diffuse in the United States. In addition to the ***twelve*** Federal agencies which support programmes related to biotechnology, many states support biotechnology centres working on state-wide or regional biotechnology development. Each centre has a different mission, funding source and series of programmes. Some support industrial research and university/industry links, others are more concerned with promoting technology transfer. At the Federal level research support is directed towards university scientists conducting basic research; applied research and development have always been considered the responsibility of industry.

US universities have played an essential role in the creation of the biotechnology industry as such. The relationship between universities and industry has become complex, including the mixture of private and public funds, resulting in research products finally covered by intellectual property protection.

Education (students, PhD post-docs, technicians)

Skilled and experienced personal is a crucial factor for establishing a strong biotechnology industry. In consequence some states and their trade associations have started initiatives across a range of the educational spectrum (Battelle Memorial Institute 2001):

- Establishment of biotechnology technician two-year associate's degree programme
- Changes in curricula at colleges and universities to better reflect the workforce needs of bioscience firms
- Outreach to bioscience companies to determine skill training and education needs

Funding of basic, industrial and interdisciplinary research

R&D is a substantial and growing enterprise in the United States with an estimated capital expenditure of 265 billion US$ for R&D in 2000 which represented 2.66 % of the nation's Gross Domestic Product (GDP). The largest share of this money (about 68 %) came from industrial firms followed by the federal government (26 %). Colleges and universities, private foundations, other non-profit institutions, and state and local governments provided the remainder (American Association for the Advancement of Science 2002).

The federal government's role is critical to the nation's science and technology enterprise as federal agencies support a majority of the nation's basic research and 58 % of the R&D performed in U.S. colleges and universities. At the same time, federally funded research at colleges and universities plays a key role in educating the next generation of scientists and engineers.

The relative priority of different areas of R&D has varied over the years, reflecting changing national priorities and the role of R&D within them. Health R&D, meanwhile, has shown practically uninterrupted growth over these years and now represents the largest single share of the civilian R&D portfolio. As an important part of research in biotechnology is located in life sciences and relates to health in particular, growth of R&D expenditures for health have a positive effect on research funds in biotechnology.

Priorities for R&D programmes generally depend on the priorities of the agencies in which they are located and the priority of the missions of those agencies. Table A9.1 shows funding programmes and budget proposes for 2003 for selected national institutions supporting research related to biotechnology. The **National Institutes of Health** (NIH) are the second-largest supporter of R&D in the federal government, after the Department of Defence and have a disproportionate impact on support for the life sciences and related fields. In their mission to promote biomedical research and other fundamental inquiries that may lead to medical advances, they are by far the largest federal supporter of basic research, applied research, and R&D at colleges and universities.

The **National Science Foundation** (NSF) plays a crucial role in the support of university research as it is the only federal agency with responsibility for research and education in all major scientific and engineering fields. Although NSF represents less than 4 % of the total federal budget for research and development, it supports roughly 50 % of all non-medical basic research at colleges and universities. In several fields, it is the lead federal source. The agency funds approximately 10,000 research, education and training projects through grants, contracts, and co-operative agreements to more than 2,000 colleges, universities, and other research and/or education organisations in all parts of the United States.

The **U.S. Department of Agriculture** (USDA) funds agricultural-related research activities at federal research laboratories, colleges, universities, and private national laboratories. Funding mechanisms include direct funding for federal research laboratories; formula funding for specific programmes at the land-grant colleges and universities; funding for research grants awarded through a competitive, peer-reviewed process to federal research laboratories, colleges, universities, and private national laboratories; and special research grants that are initiated both by USDA and Congress. The Initiative for Future Agriculture and Food Systems (IFAFS) was established in 1998 as a competitive grants programme in the Co-operative State Research, Education, and Extension Service (CSREES) for five years with a funding level of 120 million US$ per year. In FY 2002, the Agriculture Appropriations Act blocked the use of these funds.

Table A9.1: Research and Development: US Government Budget Proposes in the FY 2003

Fields supported	**Budget 2003 [Mio US$]**	**Agencies/ Institutes**	**Funding Programmes**	**Budget 2003 [Mio US$]**	**Funding Mechanisms**
National Institutes of Health (NIH) (one of 8 agencies of the Public Health Service which is part of the US **Department of Human Health and Services (DHHS))**					
Biomedical research and fundamental inquires that may lead to medical advances; large impact on support for life sciences and related fields	27,335 basic: 52 % applied: 41 %	27 institutes and centres for medical research e. g.: National Cancer Institute, National Institute of General Medical Sciences, National Institute of Biomedical Imaging and Bioengineering, National Center for Research Resources	Research Project Grants	13,748	Investigator initiated, peer-reviewed, competitive, 30 % success rate
			Small Business Innovation Research (SBIR)/ Small Business Technology Transfer (STTR) Grants	556	Competitive awards for small and medium-sized businesses; phase I: 6 months, phase II: 2 years
			Research Centers	2,466	Competitively selected
			R&D contracts	2,575	
National Science Foundation (NSF)					
Research and education in all major scientific and engineering fields (universities and colleges)	3,651	7 directorates 6 discipline oriented (biology, engineering, computer, geography, mathematics, physics), 1 Education and Human Resources	Grants contracts co-operative agreements university-industry partnerships U.S. Polar Programme	95 % for direct support 5 % administration	

Table A9.1 continued

Fields supported	**Budget 2003 [Mio US$]**	**Agencies/ Institutes**	**Funding Programmes**	**Budget 2003 [Mio US$]**	**Funding Mechanisms**
US Department of Agriculture (USDA)					
Funding of agricultural related research activities at federal research laboratories, colleges, universities and private national laboratories	2,118	Co-operative State Research, Education and Extension Service (CSREES)	National Research Initiative (NRI)	240	Grants awarded in a competitive, peer-reviewed process target: areas of new concern and promise
			Hatch Act (agricultural experiment station at 1862 land-grant universities)	180	Formula funding for specific programmes
			Special Research Grants		Initiated by USDA and Congress for target research meeting individual state agricultural needs
			Initiative for Future Agriculture and Food Systems (IFAFS)	0	Competitive research grants
		Agricultural Research Service (ARS) in-house research agency	Agricultural Genomics (sequencing plant and crop genomes)	6,9	Direct funding of federal research laboratories
Environment Protection Agency (EPA)					
Funding of research projects in ecosystems assessment and restoration, human health risk and new technologies for pollution prevention	627		Homeland Security Research		Research grants in close collaboration with local, state and global governments

Source: American Association for the Advancement of Science 2002

Tobacco settlement funds

On a federal states level 16 states use parts of their tobacco settlement funds[65] for bioscience-related research. Three states target some of the funding for technology transfer and commercialisation. In most states there is a strong focus on tobacco-related research. In addition to universities, federal laboratories e. g. DOE federal laboratories (Fermie and Argonne) in Illinois and non-profit research institutions receive parts of the funds. Ohio created a biomedical research and technology transfer trust fund and allocated 2.7 % of the first year settlement dollars to it with an increase up to 14 % in the following years (Battelle Memorial Institute 2001).

Academic Bioscience Research Centers

The knowledge and understanding that strong bioscience economies depend on strong research universities which generate bioscience discoveries resulted in an increase of state funding for biosience-related research centres. In addition, the high increase of funding support to NIH by the federal government activated the expenditure of billions of dollars in states and regions to build modern facilities and fully equipped labs with state-of-the-art instrumentation in order to compete with other regions for funding and skilled personal. Examples of publicly funded academic bioscience research centres are shown in table A9.2.

Table A9.2: Examples of publicly funded academic bioscience research centres

State	**Research Centre**	**Characteristics**
California	Institute for Bioengineering, Biotechnology and Quantitative Biomedical Research	• newly established as one of three Institutes for Science and Innovation • co-operative of the University of California and private industry • state funds totalling 100 million US$ to be matched by 200 million US$ in private funds • by 2004 more than 100 scientists involved

65 In 1998, the attorneys general of most states and the major United States tobacco companies agreed to settle more than 40 pending lawsuits brought by states against the tobacco industry. These lawsuits sought reimbursement for the expenses states had incurred for smoking-related health costs. As part of the agreement, the tobacco companies are required to make annual payments to the states in perpetuity.

Table A9.2 continued

State	Research Centre	Characteristics
Delaware	Delaware Biotechnology Institute	• founded in 1999 • housed in new 72,000 square foot research building • 180 researchers • focus on agriculture, biomaterials, human health and marine ecosystems • educational programmes in life sciences addressing governmental, academic and private needs • research consortium and incubator for biosciences companies • 85 million US$ funding from state grants, industry partners and Delaware's institutions of higher education
New York	Strategically Targeted Academic Research (STAR) Centers	• four centres with bioscience focus • 15 million US$ funding for each centre

Source: Battelle Memorial Institute 2001

A9.2.2 Commercialising biotechnology

One of the most remarkable characteristics of US biotechnology policy is the major effort the US government puts into co-operation with the private industrial sector. Besides the support for universities and governmental agencies, special federal programmes support the joint commercialisation by the public and private sector of results of federal research initiatives.

Grants for industrial research

The U.S. Small Business Administration Office (SBA) strengthens and expands the competitiveness of U.S. small high technology research and development businesses in the federal marketplace. The office assists in achieving the commercialisation of the results of both the federal research and development programmes and is mandated by the Small Business Innovation Development Act of 1982, the Small Business Research and Development Enhancement Act of 1992, and the Small Business Innovation Research Programme Reauthorization Act of 2000. The U.S. SBA plays an important role as the co-ordinating agency for the following programmes and initiatives: Small Business Innovation Research Program (SBIR) and Small Business Technology Transfer Program (STTR).

It directs the participating agencies' implementation of SBIR, reviews their progress, and reports annually to Congress on its operation.

The Small Business Development Act was passed by Congress in 1982, requiring all major federal agencies to conduct the Small Business Innovation Research Program. This calls for the Federal agencies which conduct 99 % of total US Government R&D to publish and distribute annually a comprehensive description of their R&D programmes. Each agency must also solicit research proposals from small business and fund a minimum of 1.25 % of their external research from this source.

There are no special programmes to support biotechnology SMEs, but they are eligible to apply for financial support under the Small Business Innovation Research Program (SBIR), to which the National Institute of Health (NIH) contributes significant funds. SBIR is a highly competitive programme that encourages small business to explore their technological potential and provides the incentive to profit from its commercialisation. As risk and expense of conducting serious R&D efforts are often beyond the means of many small businesses, the programme was set up to reserve a specific percentage of federal R&D funds for small business for enabling them to compete on the same level as larger businesses. Each year, ten federal departments and agencies are required by SBIR to reserve a portion of their R&D funds for award to small business (Small Business Administration 2002).

SBIR funds the critical start-up and development stages and it encourages the commercialisation of the technology, product, or service. The programme is also designed to provide a means for converting government R&D into technology, thereby increasing the commercial returns from Government research. Government funds 100 % of small firms' R&D to produce commercial products if the R&D also meets a government requirement. There is no requirement for payback or recoupment, and the programme offers world-wide commercial patent rights to the small firm for any patents resulting from the research.

Financial support is provided in three phases: the first phase provides limited funds for short-term feasibility studies – both technical feasibility and firm capability. Firms demonstrating adequate progress receive more substantial funds over one to two years under phase II for taking research ideas through to the prototype stage. phase III involves securing private funding for taking the prototype through to the market. Few small firms receive phase II grants without obtaining in advance a signed contingent follow-on funding commitment from a third party firm. Large companies and venture capital firms have become enthusiastic about the SBIR programme as a test bed for high-risk ideas (Senker et al. 2001).

The Advanced Technologies Programme (ATP), part of the National Institute of Standards and Technology, supports the high development risks of innovative technologies by providing support for research projects undertaken by companies of all sizes, working alone or in partnership with other companies, universities, federal laboratories or non-profit independent research organisations. ATP awards are competitive and made on the basis of rigorous peer-review, but proposals can only be submitted in response to specific, published calls. The proportion of costs provided by awards depends on the size of the company. For example, joint ventures involving two or more companies must pay at least half of the project costs. SMEs in single firm projects must pay a minimum of all indirect costs associated with the project. Since 1990 ATP has funded 468 projects. Over half these awards have been made to individual SMEs or to joint ventures led by an SME. Other SMEs are involved in awards to joint ventures led by larger firms (Senker et al. 2001).

Between 1994 and 1998 most ATP funding was allocated to specific programme areas. In the biotechnology area, these included Tools for DNA Diagnostics (145 million US$ funding 1994 to 1998) and a Tissue Engineering programme which commenced in 1997.

Science and technology parks

Research parks built near universities, medical centres and teaching hospitals were emerging across the U.S. in the recent years. Innovation in biotechnology highly depends on academic research. Thirty years ago academic research centres like the Harvard and Stanford University, the University of California or the Massachusetts Institute of Technology (MIT) were building first incubators in biotechnology, out of which biotech companies were founded. In order to keep up the contact with academic research, they settled nearby these centres. In the meantime, a high number of states have research parks that can or do house bioscience companies, but research parks focused exclusively on bioscience companies are found in nine states only. Some of the research parks have been publicly supported, others are private operations (table A9.3).

Table A9.3: Examples of publicly supported research parks

State	Research Park	Characteristics
Massachusetts	Massachusetts Bio-technology Research Park	• created in 1985 • includes 1 million square feet on 105 acres • more than 12 biotech companies and several non-profit and academic institutions • houses MBIdeas Innovation Center, offering wet lab space, use of existing permits, business assistance, consulting and mentoring to start-up companies
	University Park at MIT	• created in 1983 • located on 27 acres next to MIT • 1.5 million square foot of R&D space, including offices, hotel and conference centre
Maryland	Shady Grove Life Science Center	• located in Maryland's I-270 technology corridor • houses corporate tenants and the Center of Applied Research in Biotechnology, a University of Maryland teaching facility in which 11 different universities and colleges offer graduate and undergraduate courses
Colorado	Colorado Bioscience Park Aurora	• under development • 3 million square feet • affiliated with the University of Colorado • for research-oriented biomedical, biotechnology and pharmaceutical operations in multi-tenent buildings
	Bioscience Park Center	• opened in 2000 • 60,000 square foot facility • designed to house start-up companies • provision of services and specialised equipment and facilities

Source: Battelle Memorial Institute 2001

Facility costs are among the most significant expenses of a new biotechnology firm. In consequence most bioscience firms initially lease space rather than purchase it. For emerging bioscience regions it is a major challenge to offer the right amount and type of space suitable for the development and growth of biotechnological companies. To encourage the private market to invest in these facilities some states have set up economic development programmes either for constructing biotechnology facilities (e. g. tax credit in Arkansas) or to support the development or expansion of facilities of biotech firms through special financing funds (e. g. Connecticut's Biotechnology Facility Fund).

Technology transfer

There are numerous approaches by states and regions to encourage and facilitate commercialisation of research findings and to build companies from the research enterprise. In most cases some type of commercialisation and business development support to start-up companies is given and in general assistance is not limited to any particular type of technology. Assistance may cover technology assessment and technical concept analysis, engineering, testing and prototype development, market research and analysis, economic feasibility studies, strategic marketing and business plan development and access to early-stage venture capital.

Examples of programmes specifically targeted to bioscience companies are MDBio, a private non-profit corporation created by the State of Maryland and the Carilion Biomedical Institute in Roanoke, Virginia. MDBio awards funding to bioscience companies for product development and manufacturing, assists with marketing and regulatory issues and provides financing. The Carilion Biomedical Institute provides prototype development facilities (Battelle Memorial Institute 2001).

The Small Business Technology Transfer Programme (STTR), co-ordinated by the U.S. Small Business Administration Office (SBA) is an important small business programme that expands funding opportunities in the federal innovation research and development arena. Central to the programme is expansion of the public/private sector partnership to include the joint venture opportunities for small business and the nation's premier non-profit research institutions. STTR is a highly competitive programme that reserves a specific percentage of federal R&D funding for award to small business and non-profit research institution partners (Small Business Administration 2002).

Regarding technology transfer from university side, most universities have established technology transfer units in the last two decades since passage of the Patent and Trademark Amendments (P.L. 96-517), known as Bayh-Dole Act, in 1980. The Bayh-Dole Act permits universities and small businesses to elect ownership of inventions made under federal funding and to become directly involved in the commercialisation process. It also permits exclusive licensing when combined with diligent development and transfer of an invention to the marketplace for the public good (Council on Governmental Relations 1999).

Technology transfer offices support patenting of inventions and the active marketing of these patents. An example is the Office of Commercial Ventures and Intellectual Property (CIVP) at the University of Massachusetts, Amherst. The CIVP's mission is to secure continuing financial support for research at university through the development of mutually beneficial research and licensing agreements with industry partners. Tasks of the office include identification and evaluation of promising technologies within the university, guidance through the patenting process, identification of commercial partners and negotiation of research supports and commercial agreements (University of Massachusetts Amherst 1998). However, there is a great diversity among universities with respect to their patenting and technology licensing approach. Some institutions mainly intend to generate revenue by licensing and others see these units as instruments for building long-term relationships with private companies.

Collaboration between public and industrial research / Programmes to improve co-operations between research institutions and companies

One of the most important ways of technology transfer is collaboration between universities or U.S. federal laboratories and industry partners. Concerning university-industry co-operation public funding has been a major catalyst. The institutional framework structuring most university-industry research collaborations are the university-industry research centres (UIRC), which facilitate industry access to university research results, engage industry in the definition of a research portfolio and promote technology transfer to participating companies in exchange for their sustained funding. In most cases this support is matched by public funds of which the National Science Foundation takes a leading role (see table A9.1). UICRs account for roughly 50 % of all industrial funding of U.S. academic research. UICRs vary with respect to their research orientations and their disciplinary and technological focus (Abrahamson et al. 1997).

For U.S. federal laboratories, Co-operative Research and Development Agreements (CRADA) is the most important mechanism for co-operative research with industrial partners. CRADAs, authorised by the Federal Technology Transfer Act of 1986 (FTTA) to promote the transfer of government developed technology to the private sector, give permission on the one hand to laboratories to contribute staff and equipment to a project with a private partner, and on the other hand to companies to acquire patent rights arising from the co-operative research with royalties expected to be shared with the government inventors (Abrahamson et al. 1997).

A9.2.3 Creating a supportive framework for biotechnology

IPR/Patenting

Patent applications in the United States, made to the Patent and Trademark Office (USPTO) differ in important respects from those in Europe. An important difference is patent document publishing procedures. (Publication occurs when the application is made public.) In Europe patent applications are usually published 18 months after application but protection is provided from the date on which the patent application was first filed. In the US a patent application is only published if the patent is granted. This may take as long as five years. However, the American Inventors Protection Act 1999, which came into force in late 2000, will also make patent applications subject to publication 18 months after filing (Tzevdos et al. 2000). In contrast to European patent laws, where discussion of academic work prior to filing a patent can lead to the loss of patent rights, U.S. patent laws offer the possibility to apply for a patent on an invention described in a printed publication within the last year. Only if the printed publication is prior one year to filing the patent application, patents are prohibited (USPTO 1997). This regulation is especially advantageous for academic research and encourages patenting of research results at universities.

Guidelines for determining whether a gene-related patent will be granted are expected to be released soon by the US PTO. The guidelines follow similar principles to the stipulation in 98/44/EEC that DNA sequences must show utility to be patented. The USPTO guidelines will tighten former standards and demand that patent applications show "specific, credible and substantial utility for gene sequences" (Grisham 2000).

Financing

The availability of capital plays an important role in the development of the biotech industry. As the development of biotechnological products requires expensive and time-consuming research large amounts of patient capital are needed to develop and sustain the biotech industry. Generally three measures of capital flow to the biotech industry can be identified: venture capital, research alliances and initial public offerings (IPO). As start-up firms normally depend on venture capital investment and IPO financing depends on the maturity of the firm and the product that may be marketable on the stock exchange, financing also reflects different phases in the life cycle of a firm and the development of a product.

Private investment

Venture capital investment

Venture capital investment finances most biotech firms from their inception through the years of research and product development. Venture capital is a leading indicator of the development of ideas into potential businesses. Along with the valuation of public biotech companies in the second half of 1999 came an increase in venture investment in earlier stage private companies which ended in March 2000 along with the drop in the public biotech markets. Although biotech firms attracted more than 3 billion US$ in 2000, biotech accounts for only 5 % of all venture capital investment in 2000 (PriceWaterhouseCoopers 2001).

Venture capital investment in biopharmaceutical firms is concentrated within a few metropolitan areas (Boston, San Francisco, San Diego, Seattle and Raleigh-Durham), which partly reflects the presence of very active biotech investors concentrated in these areas (San Francisco, Boston, New York, Philadephia, San Diego, Chicago and Raleigh-Durham). This indicates that the availability of venture capital partly depends on the presence of local venture capital firms.

Apart from investment in biotechnology of venture groups, corporate venture capital investment in biotechnology surged in 2000. An increasing number of large pharmaceutical companies provided venture funding to biotech start-ups, a process which is indicative for an overall trend in corporate investing programmes across industries. About 20 % of all venture financing in 2000 came from corporations. Beside pharmaceutical companies, technology companies with focus on e-health and bioinformatics invest in biotechnology.

There are several differences of venture and corporate venture groups which may lead to problems if they invest in the same company: generally venture investors look for financial return on horizons of five years or less whereas corporate venture groups have horizons of five or even ten years and often measure their returns in other dimensions. Motivations of corporate investors comprise:

- Access to promising new technologies
- Access to early-stage technology rights
- Reduced risk and expense of in-house research and development
- Expanse of the pipeline
- Need to diversify and to test the relationship with a new business on a small scale
- Strategic growth
- Financial return

Forms of corporate investment:

- Direct investment through a dedicated fund
- Fund of fund investment (limited partnership in an outside fund)
- Alliance equity investment through the corporate development function (part of partnering deal/strategic alliance)

Strategic alliances

A major source of financing for biotech firms consists of research and development contracts and funding arrangements with pharmaceutical companies. Partnering offers a wide range of financing measures and other advantages to biotech companies as (Burrill & Company 2000):

- Licensing and other upfront fees to recoup start-up and early-stage R&D expenses
- Reimbursement of development expenses for partnered products/services
- "Success fees" along the way, when key risk-reduction milestones are achieved
- Royalities of profit "splits" upon product commercialisation
- Access to partner's downstream product development expertise
- Access to partners' expertise and resources in world-wide product registration and commercialisation (marketing and distribution)

Research agreements between pharmaceutical and biotech companies have grown from 5.2 billion US$ between 1990 and 1995 to 11.2 billion US$ in the period from 1996 to 2001. Only the dramatic opening of the equity markets in the second half of 1999 catapulted the value of public financings beyond that of partnering and this trend continued in 2000. Research contracts extended to biotechnology companies by pharmaceutical companies are highly concentrated within four metropolitan areas (Boston, San Francisco, San Diego, New York) accounting for four-fifth of the value of all research contracts.

Initial public offerings

Going public is another important source of financing biotechnology firms in the US. For privately held firms, going public requires undertaking an initial public offering (IPO) prior to which the firm must undergo a process of review and disclosure. Costs involved imply that only companies with relatively large-scale and/or sufficiently well developed property or products can raise funds in this fashion. Between 1998 and 2001 89 biotechnology firms made the initial filings to undertake an IPO, of which established biotechnology centres accounted for the biggest part of these IPOs (Cortright and Mayer 2002).

Public programmes providing seed and pre-seed financing

Early stage financing is perceived to be a capital gap on the private market. To overcome the shortage of pre-seed to seed-stage venture capital some states have developed programmes to address this need. Measures comprise direct investments in companies, investment in privately managed venture funds and tax incentives to encourage investment in venture capital. In some cases, universities and foundations are investing a portion of their endowments in seed and pre-seed funding for bioscience companies.

To date five states have publicly supported seed and venture funds that invest exclusively in bioscience-related companies.

Table A9.4: Publically supported venture funds in the biotech field

State	Fund	Characteristics
California	CalPERS Biotechnology Programme	• CalPERS is the largest pension fund in the U.S. • the programme is part of the CalPERS Alternative Investment Management Programme • calls for the State's employee retirement fund to invest 500 million US$ in biotechnology sector
Massachusetts	BioVentures Investors LLC	• privately managed venture fund • supported by the federal funded Massachusetts Biomedical Initiative (MBI) • investment planned in biotechnology, health care, medical devices, bioinformatics and genomics, health-related services, drug discovery
North Carolina	NC Bioscience Fund	• created by the North Carolina Biotechnology Center, a private non-profit organisation established in 1981 • managed by Eno River Capital, N.C. • provides seed capital to biotech companies • capitalised with 10 million US$ by the N.C. General Assembly • actual volume: 25 million US$ by the help of outside investors
Ohio	EBTC BioInvestment Fund	• support of business growth activities in biomedical, biotechnology and health care information sectors • fund seeks a return by investing in technology-based companies with significant market potential for which EBTC's involvement is critical to qualify the company for conventional investment or to maintain an Ohio presence
Wisconsin	State of Wisconsin Investment Board	• multi billion pension fund of the state • awarded 50 million US$ to two privately funded Wisconsin venture capital funds (Manson Wells, Venture Investors Management), managed by professional venture capitalists • funds to be used for biotechnology-related investment in companies of the state

Source: Battelle Memorial Institute 2002

Tax reduction

US states continue to use their tax structures strategically to encourage private investment in biotechnology firms, to ease the tax burden on such firms and/or to even the co-operation of biotechnology firms with traditional industries. The majority of the states have R&D tax credits. But other ways to meet the needs of biotechnological companies are (Battelle Memorial Institute 2001):

- *Sales and use tax exemptions and/or deferral*: provision of additional R&D capital by exempting the applicable sales and use taxes paid on purchases on R&D and manufacturing materials.
- *Investment tax credits*: credit for manufacturing modernisation and upgrade expenses; sales tax exemptions for computer and R&D equipment purchases.
- *Capital gains tax cuts*: incentive for individual investors in biotechnology companies by cutting the state tax rate or by a rollover provision that allows the investor to defer tax if the stock is sold and invested in another qualifying company for at least one year.
- *Net operating loss provisions*: some states allow net operating losses to be carried forward for up to 20 years.
- *Tax credit transferability*: some states allow biotechnology companies to transfer tax benefits to generate capital and assist technology investment in the state.
- *Incentives for specific industries*: provision of tax credits for activities like job creation, training, facility renovation in biotechnology.

A9.3 Conclusions

In the United States biotechnology is a rapidly growing industry. A number of factors are advantageous and stimulating for the growth of the biotech industry.

- Large resources in science and technology concerning funding and people: with 27,335 million US$ proposed budget for Fy 2003, the National Institute of Health (NIH) is the second largest supporter of R&D in the U.S. and has great impact on support of biotechnological research. The enormous size of this budget becomes obvious if it is compared with public funding for biotechnology in Europe. For the period of the 4th Framework Programme (1994 to 1998) European member states together provided in total about 10 billion € for biotechnology R&D.
- Large and established market for venture financing and many measures and programmes initiated by federal states including tax reductions or investments in special funds for financing of start-up biotech firms.

- Creation and public support of science parks, housing biotech companies, venture groups, networking organisations, academic institutions and supporting organisations or industries on the same area.
- Favourable patenting and technology transfer environment: The Bayh-Dole Act permits universities and small businesses to elect ownership of inventions made under federal funding and to become directly involved in the commercialisation process. U.S. patent laws offer the possibility to apply for a patent on an invention described in a printed publication within the past year.

A10 References

Abramson, H. N.; Encarnação, J.; Reid, P. P.; Schmoch, U. (Ed.) (1997): Technology transfer systems in the United States and Germany. Lessons and perspectives. Part I: Overview and comparison. Washington, D.C.: National Academy Press, 1-60

AKA (2000): Annual report. The Academy of Finland

American Association for the Advancement of Science (2002): AAAS Report XXVII. Research and development FY 2003. http://www.aaas.org/spp/rd/rd03main.htm

Anonymous (2002): Enterprise development in Estonia. Report provided by the Ministry of Economic Affairs and Communications

Archimedes Foundation (2002): Esis. http://www.esis.ee/ist99/archimedes.html

Archimedes Foundation (2002): Estonian participation in the European Union Fifth RTD Framework Programme (FP5)

AS Silmet Group (2002): http://www.silmetgroup.com/boci_group.html

Asper Biotech (2002): Aspers biotech's corporate vision and mission. Press release. http://www.asperbio.com/company.htm

Bank of Estonia (2000): Annual report 2000. Tallinn

Barbagallo, F.; Trench, B. (1999): Genes on the agenda. School of Communications, Dublin City University

Battelle Memorial Institute (2001): State government initiatives in biotechnology 2001. Report prepared for the Biotechnology Industry Organisation (BIO). http://www.bio.org/tax/battelle.pdf

Benedictus, J. N. (1999): National Report of Finland. In: Inventory of Public Biotechnology R&D Programmes in Europe

Bikales, N.M. (1996): Science in Estonia. NSF Europe, Report 83

BMBF (Ed.) (2000): Beschäftigungspotenziale im Bereich Bio- und Gentechnologie. Bericht des Fachdialogs im Rahmen des Bündnisses für Arbeit, Ausbildung und Wettbewerbsfähigkeit. Bonn: Bundesministerium für Bildung und Forschung

BMBF (2001): Biologische Forschung und Technologie, Rahmenprogramm des Bundesministeriums für Bildung und Forschung. Technologienachrrichten 2/3-2001

BMBF (2001): Rahmenprogramm Biotechnologie – Chancen nutzen und gestalten. Bonn

BMFT (1990): Biotechnologie 2000, Rahmenprogramm der Bundesregierung. Bonn

Boston Consulting Group (2001): Position und Perspektiven von Österreich in der Biotechnologie. Erfolgsfaktoren für eine internationale Positionierung

Burrill and Company (2000): Biotech 2000 report

Canning, S. (2000): Ireland embraces biotechnology. Nature Biotechnology 18, March 2000

Cooper and Whelan (1973): Science, technology and Industry in Ireland. Dublin, Ireland: Stationary Office

Corthright, J.; Mayer, H. (2002): Signs of life. The growth of biotechnology centers in the U.S. http://www.thbi.org/ir/tx/industry/econ_dev/brookings_biotech.pdf

Council on Governmental Relations (1999): The Bayh-Sole Act. A guide to the law and implementing regulations. http://www.cogr.edu/bayh-dole.htm

De Jager, D.; van Looy, B.; Hinoul, M. (2001): High tech venturing in Estonia: Background report for the ESTPIN programme. Amsterdam: Technopolis BV, Leuven: KU Leuven R&D

Deeds, D. (2001): The role of R&D intensity, technical development and absoptive capacity in creating entrepreneurial wealth in high technology start-ups. Journal of Engineering and Technology Management 18, 29-47

Deeds, D.; DeCarolis, D.; Coombs, J. (1999): Dynamic capabilities and new product development in high technology ventures: An empirical analysis of new biotechnology firms. Journal of Business Venturing 15, 211-229

Dempsey, N. (1999): National consultation on genetically modified organism and the environment. Policy Statement

Department of Trade and Industry (1996): Bioguide. London: DTI

DG Enterprise of the European Commission (2001): Innovation policy issues in six candidate countries: the challenges. Luxembourg: Office for Official Publications of the European Communities

Dunwell, J. M. (1999): Transgenic crops: the next generation, or an example of 2020 vision. Annals of Botany 84, 269-277

Edquist, C. (1997): Systems of innovation approach - their emergence and characteristics. Introduction. In: Edquist, C. (ed.): Systems of innovation – technologies, institutions and organisations. London, Washington D. C.: Printer Publishers, 1-35

EGeen (2002): EGeen International completes $4.25 million in first venture round. Press release. www.egeeninc.com

Enzing, C. M.; Benedictus, J. N.; Engelen-Smeets, E. et al. (1999): Inventory of public biotechnology R&D programmes in Europe. Luxembourg: Office for Official Publications of the European Communities

Ernst & Young (1998): Aufbruchstimmung 1998. Erster Deutscher Biotechnologie Report. Stuttgart und Mannheim

Ernst & Young (2000): The economic contributions of the biotechnology industry to the U.S. econonmy

Ernst & Young (2001): United Kingdom: Strong Biotech Market Promotes Regulatory

Ernst & Young: Annual European Life Science Reports, several years. Cambridge: Ernst & Young

Ernst & Young: Changes while seeking new funding opportunities. http://www.ey.com/GLOBAL/gcr.nsf/International/UK~Global_Market_-_Healthcare

Estonian Genome Project (2002): Main provisions of the Human Genes Research Act. http://www.geenivaramu.ee/?lang=eng&sub=64

Estonian Institute for Futures Studies (2001): Innovation policy in six candidate countries: The challenges. Innovation policy profile: Estonia. Louvain la Neuve

Estonian Investment Agency (EIA) (1999): Wood processing – the third largest industry in Estonia. http://www.eia.ee/pages.php3/020301

Estonian Investment Agency (EIA) (2001a): Food-processing industry 2001. Becoming an EU-adapted food-processing industry. Tallinn: EIA

Estonian Investment Agency (EIA) (2001b): Chemical industry 2001. Estonian chemical industry – an exporting industry with high concentration of FDI. Tallinn: EIA

Estonian Regional Development Agency (2002): Start-up aid. Programme information. http://www.erda.ee/english/en_supnet-start.html

Estonian Technology Agency (2002a): Annual report 2001. Tallinn

Estonian Technology Agency (2002b): Projects financed. http://www.estag.ee/4641

Estonian Trade Council (2002): Review of furniture industry in Estonia. http://www.etc.ee/furniture/?review

European Private Equity and Venture Capital Association (EVCA): EVCA yearbook. Different years. Zaventem: EVCA

Eurostat (2002): R&D and innovation statistics in candidate countries. Luxembourg: European Communities

FIT Biotech PLC (2002): FIT Biotech acquires a share of Quattromed. Press release. http://www.fitbiotech.com/pressrel_23_09_02.htm

Foley, A. (1991): Interpreting output data on overseas industry. Overseas industry in Ireland. Dublin, Gill and Macmillin

Foley, A.; Griffith, B. (1991): Indigenous manufacturing enterprises in a peripheral economy and the single market: The case of the Republic of Ireland. Regional Studies 26, 4, 375-386

Foley, A.; Griffith, B. (1994): Education, training and the promotion of high quality entrepreneurs in the Republic of Ireland. 4th Internationalising education and training Conference, Stirling, Scotland

Foley, A.; McAleese, D. (Eds.) (1991b): Overseas industry in Ireland. Business and economics research series. Dublin: Gill and Macmillin

Forbairt (1997): Intellectual property & licensing for third level colleges. Enterprise Ireland

Gambardella, A.; Orsenigo, L.; Pammolli, F. (2000): Global competitiveness in pharmaceuticals. A European perspective. Report prepared for the DG Enterprise of the European Commission. Pisa, Milan, Siena

Giessler, S.; Reiss, T. (1999): National report of Germany. In: Enzing, C. M. et al. (Eds.): Inventory of public biotechnology R&D programmes in Europe. DE-1-DE-40

Grindex (2001): Grindex and Tallinn Pharmaceutical Company sign concern agreement. http://www.grindeks.lv/news/new10.html

Grisham, J. (2000): New rules for gene patents. Nature Biotechnology 18, 921

Gristock, J.; Senker, J. (1999): Public science & wealth creation in Britain. An information booklet prepared for the British Council. Manchester

Grupp, H. (Ed.) (1995): Technologie am Beginn des 21. Jahrhunderts. Heidelberg: Physica-Verlag

Grupp, H.; Schmoch, U. (1999): Patent statistics in the age of globalisation: new legal procedures, new analytical methods, new economic interpretation. Research Policy 28, 377-396

Hermans, R., Luukkonen, T. (2002): Findings of the ETLA survey in Finnish biotechnology firms. Discussion papers No. 819

Hernesniemi, H. (2000): Evaluation of Estonian innovation system. PHARE report: Support to European integration process in Estonia (No. ES 9620.01.01)

Hinze, S.; Reiss, T.; Dominguiez-Lacasa, I.; Wörner, S. (2001): Einfluss der Biotechnologie auf das Innovationssystem der pharmazeutischen Industrie. Karlsruhe: Fraunhofer ISI

Inter-Departmental Group Report on Modern Biotechnology (2000): Irish Government report. Dublin: Government Publications Office. http://www.entemp.ie/publications.htm

Institute of Health and Consumer Protection (IHCP) (2002): Deliberate field trials. http://biotech.jrc.it

James, C. (2001): Previous: Global review of commercialised transgenic plants 2001. Itaca, NY: International Service for the Acquisition of Agri-Biotech Applications (ISAAA)

Jungmittag, A.; Reger, G.; Reiss, T. (2000): Changing innovation in the pharmaceutical industry. Berlin, Heidelberg, New York: Springer

Kerr, A. (1996): The evolution of science and technology policies in Ireland 1963-1995. Dublin City University

Kirby, J. (1999): The public, policy and GMO's. M.Sc. Thesis. School of Communications, Dublin City University

Kline, S. J.; Rosenberg, N. (1986): An overview on innovation. In: Laudan, R.; Rosenberg, N. (Ed.): The positive sum strategy. Harnessing technology for economic growth. Washington D. C.: National Academy Press, 275-306

Kurik, S.; Lumiste, R.; Terk, E; Heinlo, A. (2002): Innovation in Estonian enterprises 1998-2000. Tallinn: Foundation Enterprise Estonia

Lähteenmäki, R. (2002): Finnish biotechnology, built on solid foundations. Nature 20, 437-440

Lee, K. B.; Cooper, W. (2001): Big pharma, IT increasing corporate VC investment in biotech. In: Ernst and Young: Focus on fundamentals. The biotechnology report

Lemola, T.; Palmberg, C.; LaPointe, K. (2000): European trend chart on innovation. Country report: Finland. European Commission

Lundvall, B. A. (1988): Innovation as an interactive process – from user-producer interaction to the National System of Innovation. In: Dosi, G. et al. (Ed.): Technical change and economic theory. London: Pinter, 349-369

Lundvall, B. A. (Ed.) (1992): National Systems of Innovation: Towards a theory of innovation and interactive learning. London: Pinter

Martin, P. (1999): The national report of Ireland. In: Inventory of public biotechnology R&D programmes in Europe, Vol. 2. Luxembourg: Office for Official Publications of the European Communities

Martin, P. A. (1999): The national report of the UK: Inventory and analysis of biotech programmes and related activities in all countries participating in the Biotechnology Programme 1994-1998,. Brighton: SPRU

Martinson H. (1995): The reform of R&D systems in Estonia. Estonian Science Foundation: Tallinn

Menrad, K.; Agrafiotis, D.; Enzing, C. M.; Lemkow, L.; Terragni, F. (1999): Future impacts of biotechnology on agriculture, food production and food processing – A Delphi survey. Heidelberg: Physica-Verlag

Menrad, K.; Hinze, S.; Menrad, M.; Zimmer, R. (2001): Entwicklungskonzept "Biotechnologie/Medizintechnik" für den Großraum Hannover. Beiträge zur regionalen Entwicklung Nr. 91 A. Hannover: Kommunalverband Großraum Hannover

Ministry of Agriculture (2002): Agriculture and rural development. Overview 2002. Tallinn

Ministry of Economic Affairs and Communications (2002): Competence Centre Programme. Programme document. Tallinn

Moser Jones, M. (2001): Estonian microarray start-up hopes to capture SNP market. http://www. asperbio.com/press.htm

Nelson, R. R. (Ed.) (1993): National innovation systems: a comparative analysis. New York: Oxford University press

OECD (1997): Main science and technology indicators. Vol. 1997/2, Paris

OECD (2001): Biotech database. http://www.olis.oecd.org/bioprod.nsf

OECD (2001a): Statistical definition of biotechnology. http://www.oecd.org/oecd/pages/document/print_template/0,3371,EN-document-27-nodirectorate-no-1-31006-27---,00.html. Paris:Oecd

OECD (2002): Main science and technology indicators. Vol. 2002/1, Paris

O'Huallachain, B. (1984): Input-output linkages and foreign direct investment in Ireland. International Regional Science Review 9, 3, 185-200

O'Malley, E. (1985): The problem of late industrialization and the experience of the Republic of Ireland. Cambridge Journal of Economics 9

PEW (2001): Harvest on the horizon: future uses of agricultural biotechnology. PEW Initiative on food and biotechnology

Phare (1999): The state of small business in Estonia: Report 1998. PHARE support to SME development in Estonia. Tallinn

PHRMA (2001): New drug approvals in 2000. http://www.phrma.org

Price Waterhouse Coopers (2001): Money tree survey. http://www.pwcmoneytree.com

Quattromed (2002): Company information. http://www.quattromed.com

Sager, B. (2001): Scenarios on the future of biotechnology. Technological Forecasting & Social Change 68, 109-129

Scandinavian Care Consultants AB (2002): Tartu Biotechnology Park. Abstract from the feasibility study. Stockholm

Schienstock, G.; Tulkki, P. (2001): The fourth pillar? An assessment of the situation of the Finnish biotechnology. Small Business Economics 17, 105-122

Schmoch, U. (1999): Eignen sich Patente als Innovationsindikatoren? In: Boch, R. (ed.): Patentschutz und Innovation in Geschichte und Gegenwart. Frankfurt: Peter Lang, 113-126

Science and Society (2002): National regulations related to ethical issues in science and research: Estonia. http://www.scienceandsociety.net/estonia.html

Secretariat of the Research and Development Council (2002): Knowledge-based Estonia. Estonian strategy for research and development. Tallinn: Ministry of Education, Ministry of Economic Affairs, Estonian Academy of Sciences

Senker, J.; Brady, M.; van Zwanenberg, P. (2000): European Biotechnology Innovation System. UK Report. Brighton: SPRU

Senker, J.; van Zwanenberg, P.; Reiss, T.; Wörner, S. et al. (2001): European biotechnology innovation system. Final report. Brighton: SPRU (University of Sussex)

Sild, T.; Mullari, T. (2001): Population based genetic research: Estonian answer to the legal challenge. European Journal of Health Law 8, 363-371

Sinani, E.; Meyer, K. (2002): Identifying spillovers of technology transfer from FDI: the case of Estonia. Centre for East European Studies. Copenhagen Business School

Small Business Administration (2002): Description of the Small Business Innovation Research Program (SBIR). http://www.sba.gov/SBIR/indexsbir-sttr.html

State Agency of Medicine (2002): Medical devices. http://www.sam.ee/index.aw?section=213

Statistical Office of Estonia (2002): www.stat.ee

Statistisches Bundesamt (2001): Statistisches Jahrbuch. Wiesbaden

Tallinn Pharmaceutical Company (2002): Sales. http://farma@tft.ee/eng/myyk.php

Tartes, U. (1999): Science reform in Estonia – results and experience. Presentation at the Annual Conference of Lithuanian Scientific Society 9th October, 1999

Tartu Science Park (2001): Green Paper. Co-operation platform for innovative entrepreneurship support by national, regional and local actors. http://park.tartu.ee./greenpaper/eng/

Tartu Science Park (2002): Companies. http://www.park.tartu.ee/ttp/companies.php

TEKES (2000): Tekes annual review

TEKES (2001): Tekes annual review

Tiits, M.; Kattel, R.; Kalvet, T.; Kaarli, R. (2002): Competitiveness of Estonian economy and future outlooks. Internal working paper of the Research and Development Council. Tallinn

Trend Chart: EC Overview of innovation policy measures available in the Trend Chart data. http://trendchart.cordis.lu/Datasheets/index.cfm?

Tsevdos, E. J.; Toffenetti, J. L.; Wilson, M. L. (2000): Will publication of patent applications really affect biotechnology? Nature Biotechnology 18, 795-796

Tulkki, P.; Järvensivu, A.; Lyytinen, A. (2001): The emergence of Finnish life sciences industries. SITRA reports series

University of Massacusetts Amherst (1998): Office of Commercial Ventures and Intellectual Property. http://www.umass.edu/research/cvip/homeuni.html

US Patent aand Trademark Office (USPTO) (1997): General information concerning patents. Washington: US Government Printing Office

Vaheri, A., Akerman, K., Finne, J. (2000): Research evaluation on genetics, physiology, microbiology and molecular biology. Joint final report. www.ekek.archimedes.ee/eval/genetics-physiology.htm

van Beuzekom, B. (2000): Biotechnology statistics in OECD member countries: an inventory. Paris: OECD

van Beuzekom, B. (2001): Biotechnology statistics in OECD member countries: compendium of existing national statistics. STI Working papers 2001/6. Paris: OECD

Verband Forschender Arzneimittelhersteller e.V. (VFA) (2002): Statistics 2002. Frankfurt/M.: VFA

Wess, L. (2002): Northern lights. BioCentury 10, 34, A1-A7

Wörner, S.; Reiss, T.; Menrad, M.; Menrad, K. (2000): European Biotechnology Innovation Systems. Case study Germany. Karlsruhe: Fraunhofer Institute Systems and Innovation Research

Wörner, S.; Reiss, T. (2001): The direct and indirect impacts of new technologies on employment: The example of the German biotechnology sector. Science and Public Policy 28, 5, 371-380