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# **Research on the Estonian biotechnology sector innovation system**

Final report submitted to Enterprise Estonia, Tallinn

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## 1. Introduction and targets of the project

Modern biotechnology<sup>1</sup> is considered as one of the key technologies of the 21<sup>st</sup> 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 21<sup>st</sup> 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 predestined 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

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<sup>1</sup> 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). Therefore 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 following 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<sup>2</sup>) 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

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<sup>2</sup> 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 IMCB 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 had 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 seminars 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 seminars 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 Agrobiotech 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 extent 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.

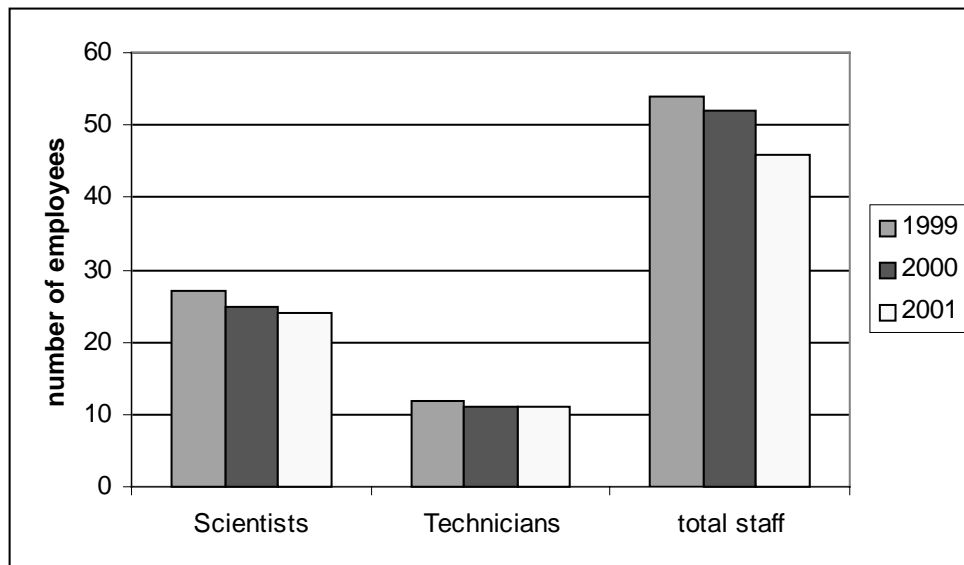
To increase public perception of science two series of seminars are carried out with the focus on "Sciences for Society" and "New Trends and Science" by the Academy of Sciences. However, the public interest is often rather low even though well-known institutes and speakers are invited. Information material 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 4<sup>th</sup> 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 institutions 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
Finland	4
European Union	2
USA	1
United Kingdom	1
Switzerland	1
Netherlands	1
Latvia	1
Germany	1
France	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				Sum
		Tallinn	Tartu	Rest of Estonia	Outside Estonia	
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

<b>Scope of co-operation</b>	<b>% of institutes</b>
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	

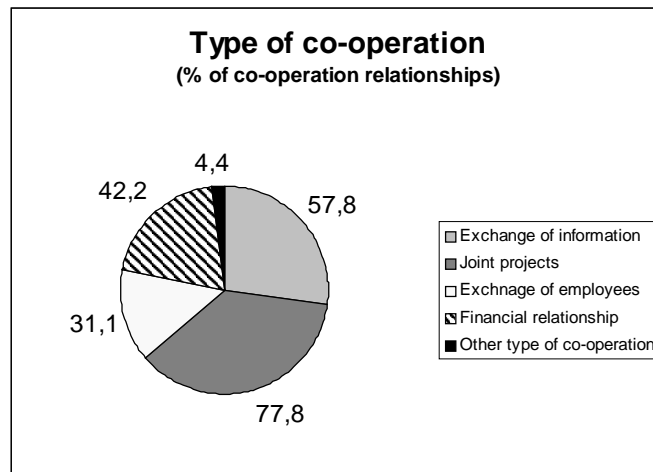
Source: Fraunhofer ISI 2002

#### *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).

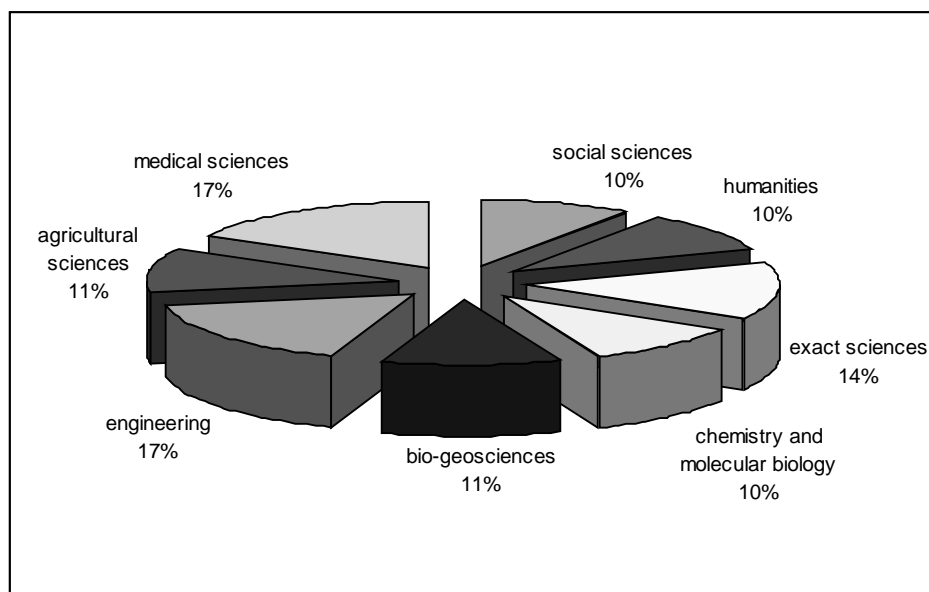
Apart from these national and European funding opportunities there are some regional activities, especially in respect to technology transfer (SPINNO project at Tallinn Technical University) and the hiring of qualified staff (repatriation fund in Tartu).

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 5<sup>th</sup> 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

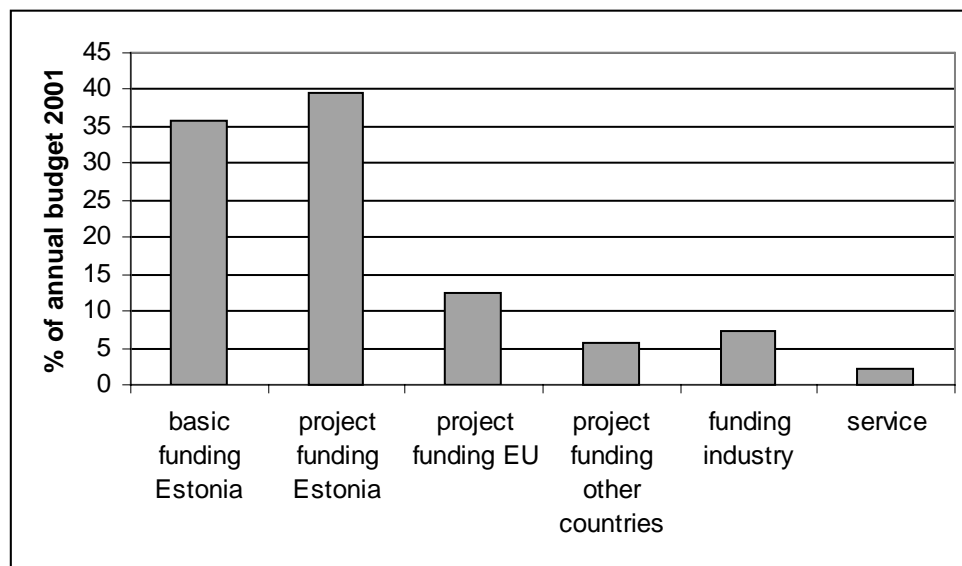
	<b>1999</b>	<b>2000</b>	<b>2001</b>
Annual average budget (mio EEK)	6.628	7.377	8.582
Inflation rate	3.1 %	3.9 %	5.5 %
Net increase	-	7.1 %	10.2 %

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.

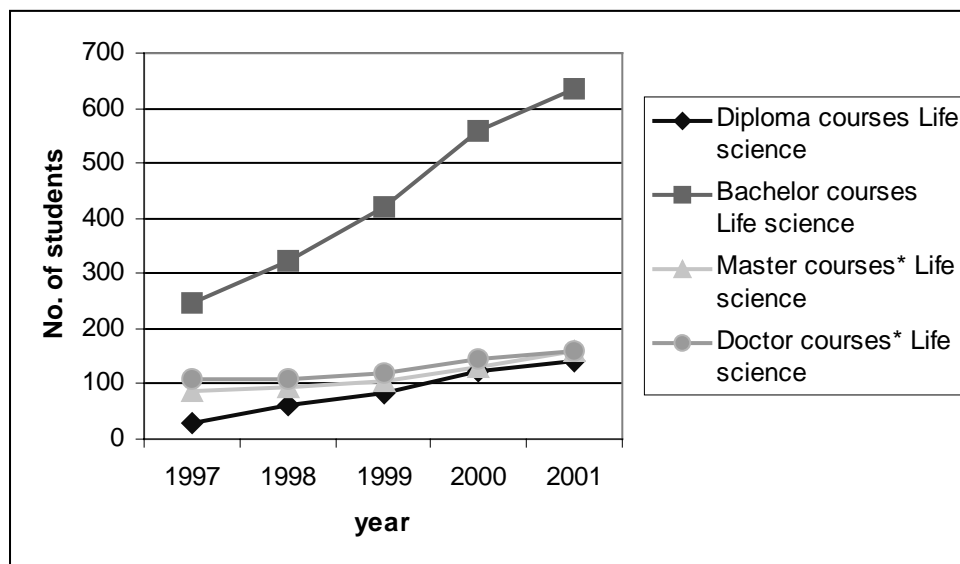
### 2.1.6 Education and training possibilities

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.

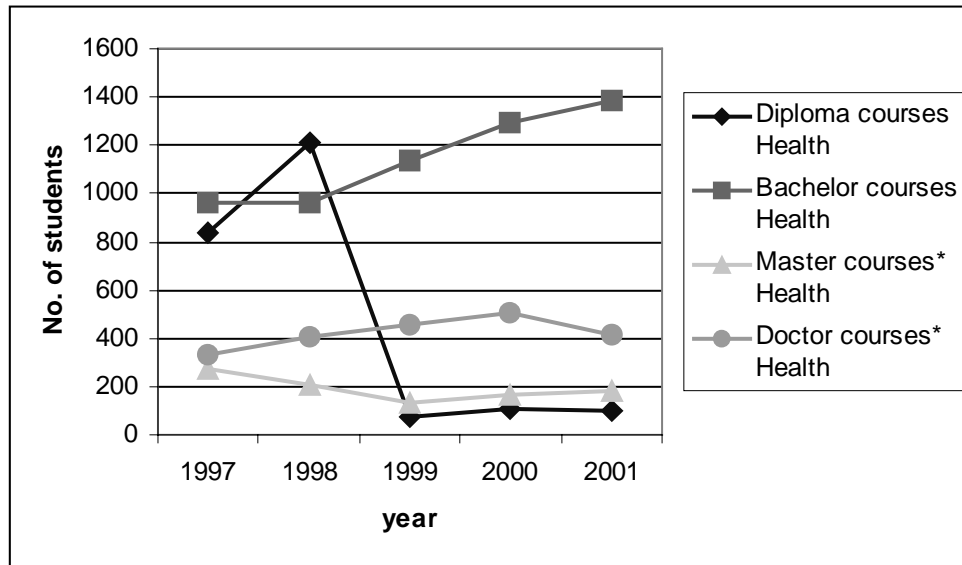
Analysing the number of students in disciplines related to the biotechnology innovation system elucidates a trend that may be problematic for the further scientific and commercial development of biotechnology in Estonia. On the one hand, the number of students in the life science sector rose constantly 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-exciting 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)

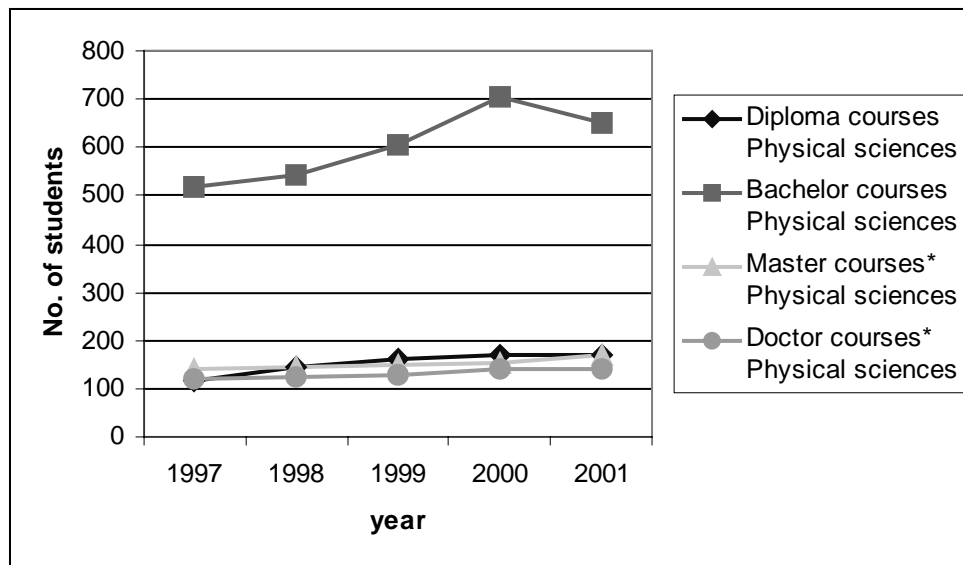
Figure 2.6: Student numbers in medicine



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

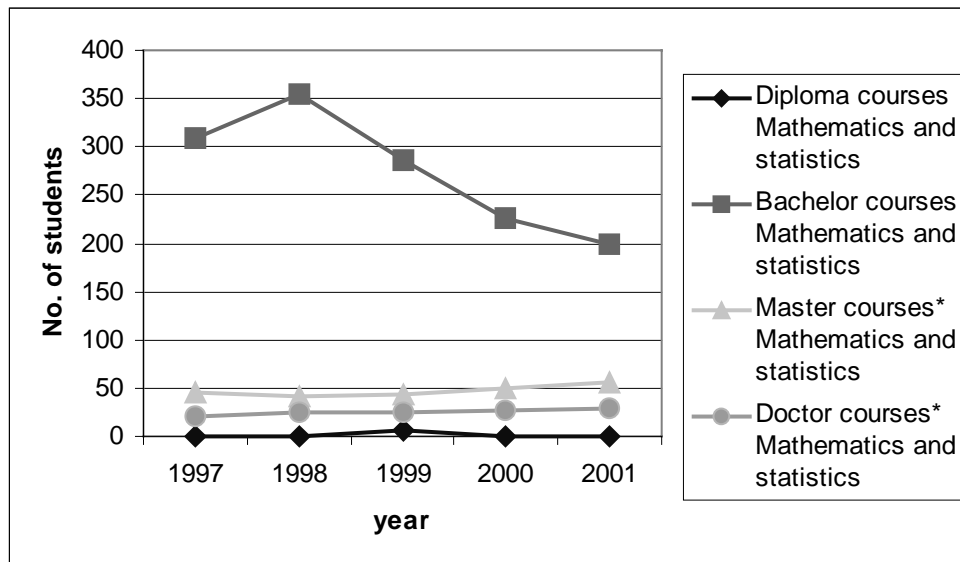
Both undergraduate and graduate student numbers in physics and mathematics decreased (figures 3.17, 3.18) in the last five years. This trend was agreed during the interviews and seen as problematic for the mid-term development of biotechnology as well as its potential application industries. The situation 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 of students in physical sciences



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

Figure 2.8: Number of students in mathematics and statistics

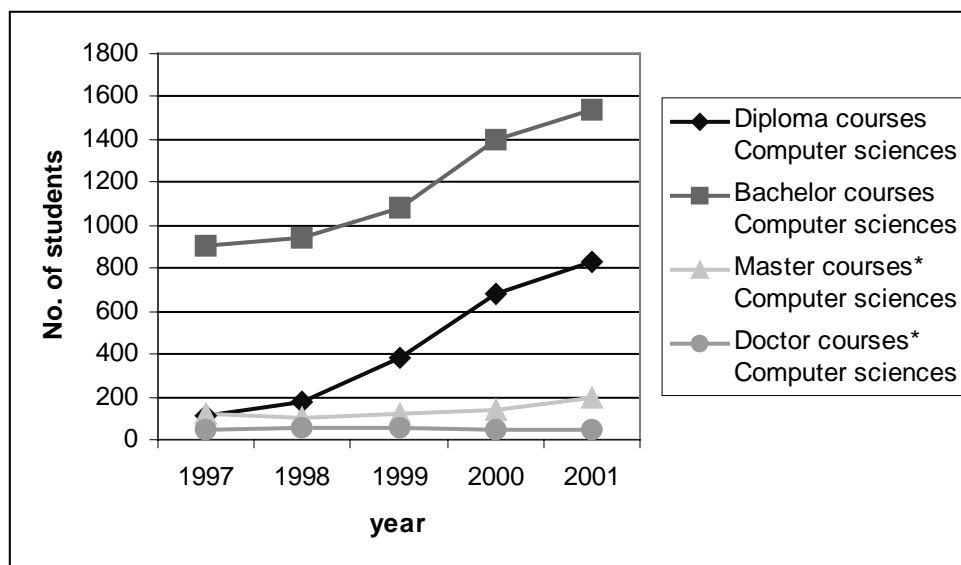


Source: Statistical Office of Estonia 2002 (\* Master courses include internship enrolment and doctor courses include residency enrolment)

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

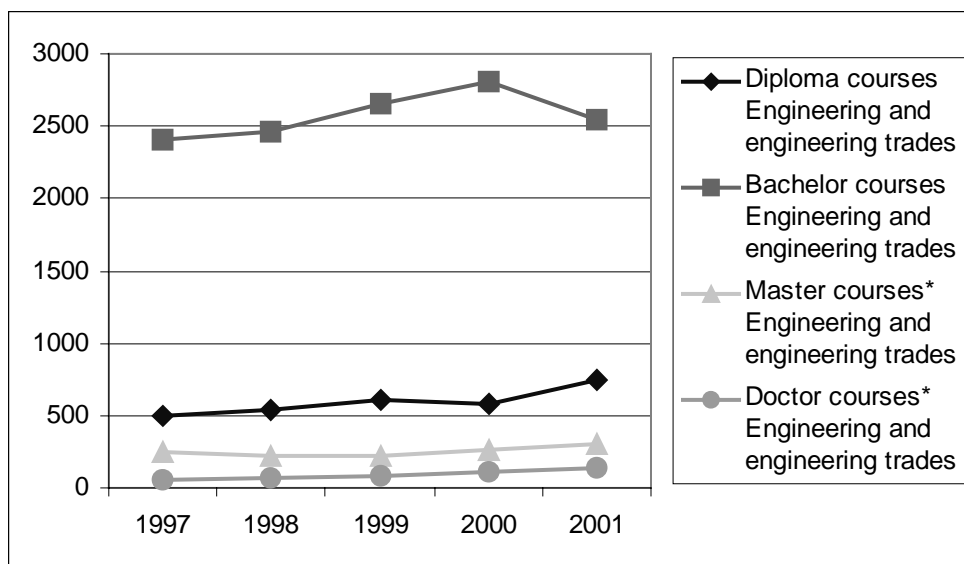
recent years (figure 2.9). This development most probably was influenced by the rather positive development of the IT industry in Estonia in the recent years. Similar trends can be registered in other European countries.

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)

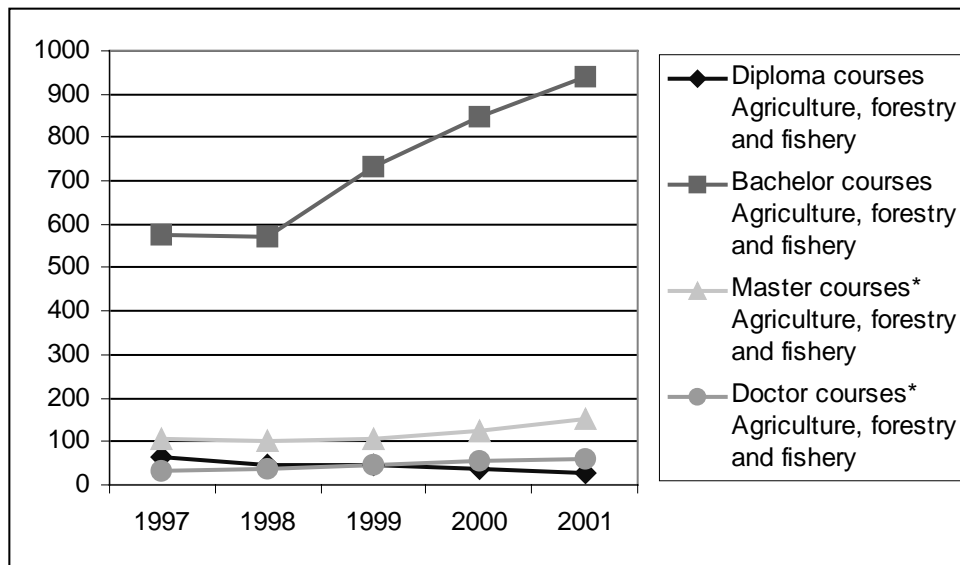
Figure 2.10: Number of students in engineering



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**

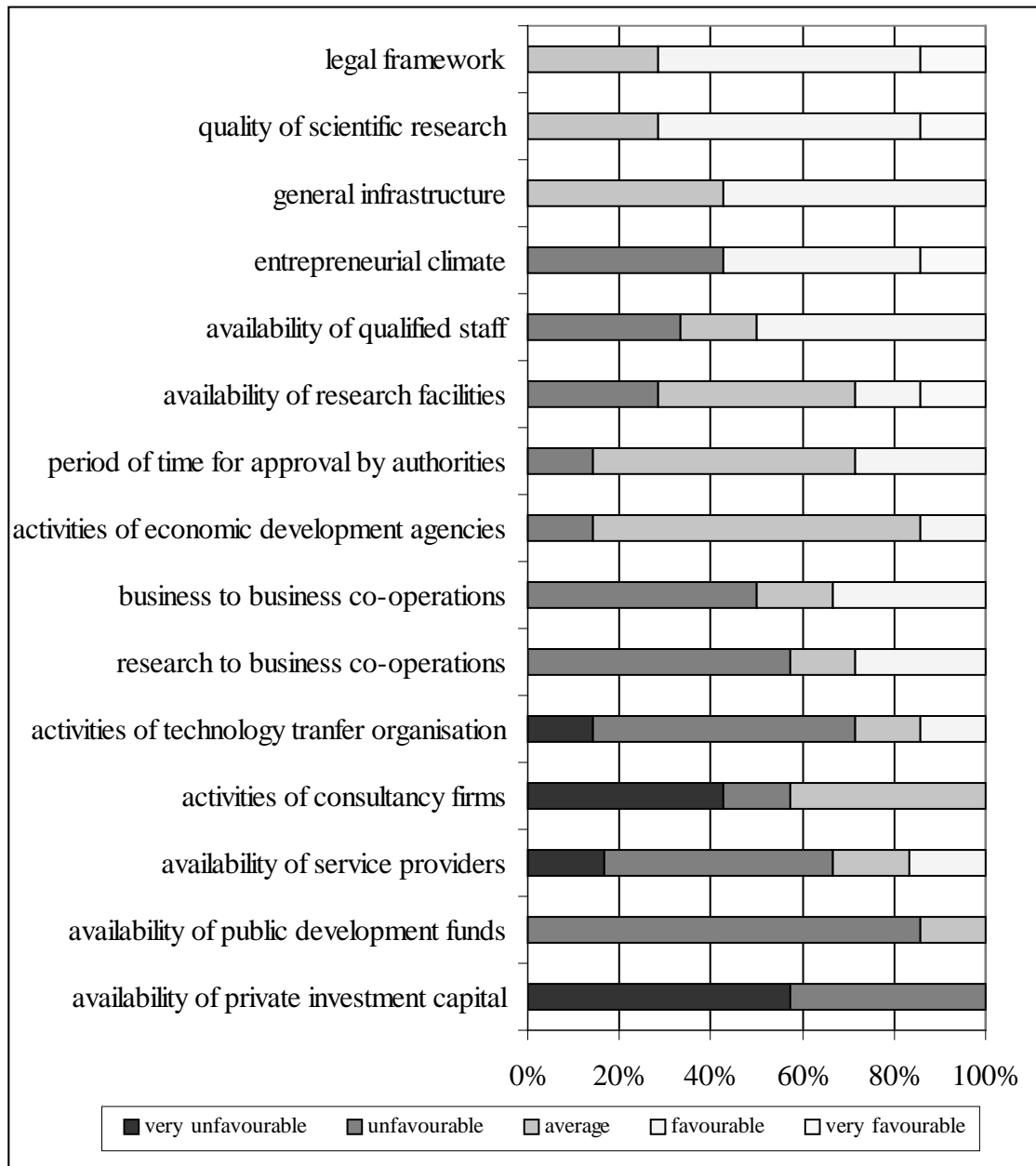
Good framework conditions are crucial for sustainable development of a sector. The biotechnology-related research institutions were asked to assess various aspects of framework conditions. The picture revealed both very positive conditions such as the legal framework and major hindrances, which pertain 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<sup>3</sup>) 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.

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<sup>3</sup> Asper and Biodata are closely interrelated and were represented by the same person.

Table 2.5: Biotech companies in Estonia

Company	Field of activity	Location	Founding year	No. of employees				VC acquired
				1-2	3-4	5-9	>10	
Core biotech companies <sup>1)</sup>								
AS PROEKSPERT/BIOEKSPERT <sup>2)</sup>	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

Company	Field of activity	Location	Founding year	No. of employees				VC acquired
				1-2	3-4	5-9	>10	
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				
Estbiotech 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 where 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)

<b>Technology competency</b>	<b>No. of firms</b>
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<sup>4</sup> (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<sup>5</sup>

No. of employees	1999 (N=8)	2000 (N=9)	2001 (N=10)	2002 <sup>1)</sup> (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

<sup>4</sup> 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.

<sup>5</sup> 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<sup>6</sup> of them generated profits while about 20 % had to face losses.

Table 2.8: Turnover of biotech companies

<b>Turnover per year<sup>1)</sup></b>	<b>1999 (N=8)</b>	<b>2000 (N=8)</b>	<b>2001 (N=16)</b>
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

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<sup>6</sup> 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 %<sup>7</sup> 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.

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<sup>7</sup> 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<sup>8</sup>. 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.

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<sup>8</sup> 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.

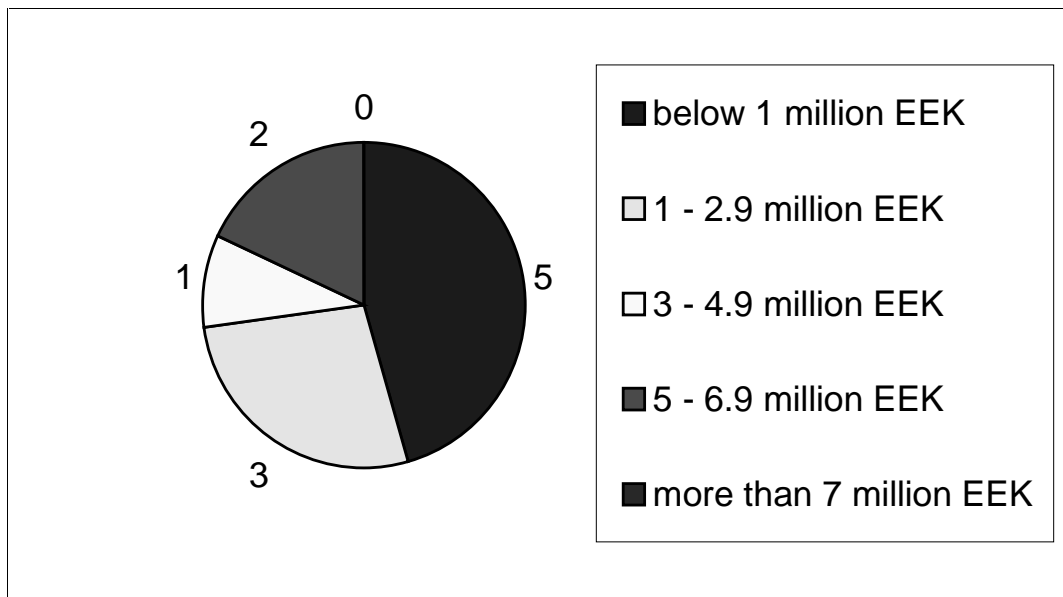
Table 2.10: Proportion of exports of biotech products or services in 2001

<b>Proportion of exports</b>	<b>Number of companies</b>
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 where technicians are trained. Only recently a new curricula for technicians was introduced at the R apina 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 R apina 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)

<b>Protection method</b>	<b>Manu- facturing</b>	<b>Services</b>	<b>10-49 employees</b>	<b>250+ employees</b>
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 attractiveness 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

<b>Country</b>	<b>Frequency</b>
Finland	4
Germany	2
Sweden	2
USA	2
France	1
Italy	1
Korea	1
Lithuania	1
Netherlands	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						

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

<b>Purpose of co-operation</b>	<b>% of companies</b>
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

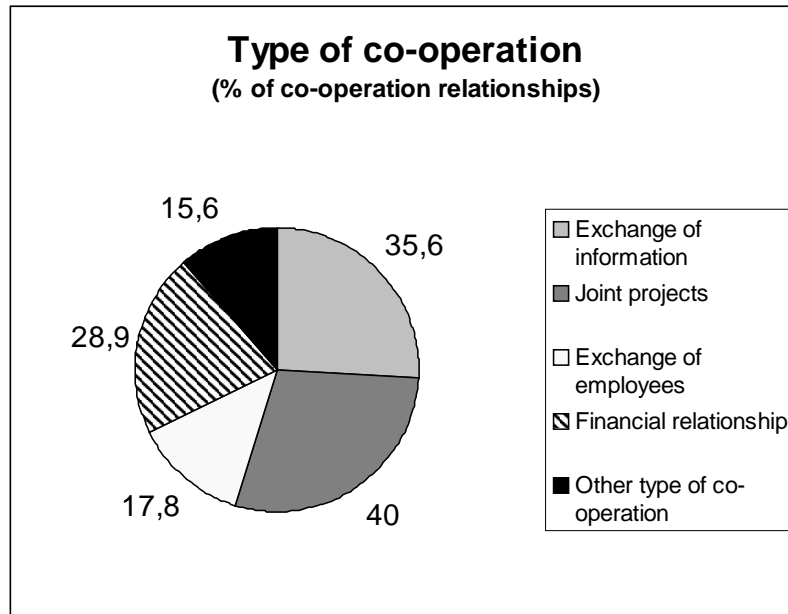
The spectrum of the collaboration purposes of the Estonian companies is also similar to the Hanover region, where scientific questions, the transformation of knowledge into products and contract manufacturing were also the most important purposes, followed by marketing and distribution of products (Menrad 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 then 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<sup>2</sup> 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<sup>2</sup> 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 from 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<sup>9</sup> 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

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<sup>9</sup> 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.

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.

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 5<sup>th</sup> 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 5<sup>th</sup> 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*

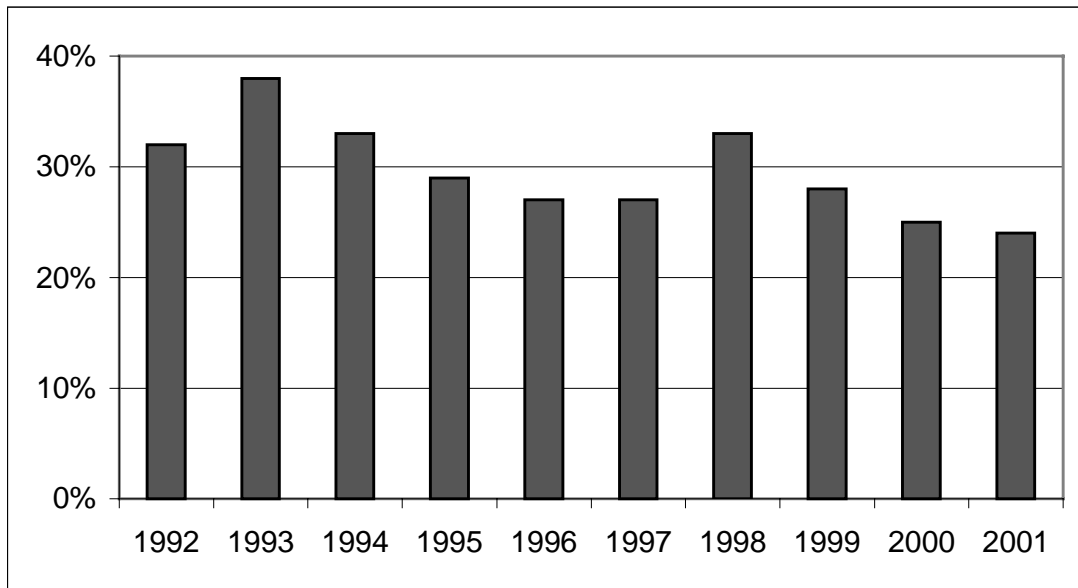
Since the independency of Estonia, the food-processing industry has been transformed from large-scale production units whose food production was mainly targeted to the Soviet Union market to a widely diversified industry branch with a high number of SMEs. The food-processing industry has traditionally 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)

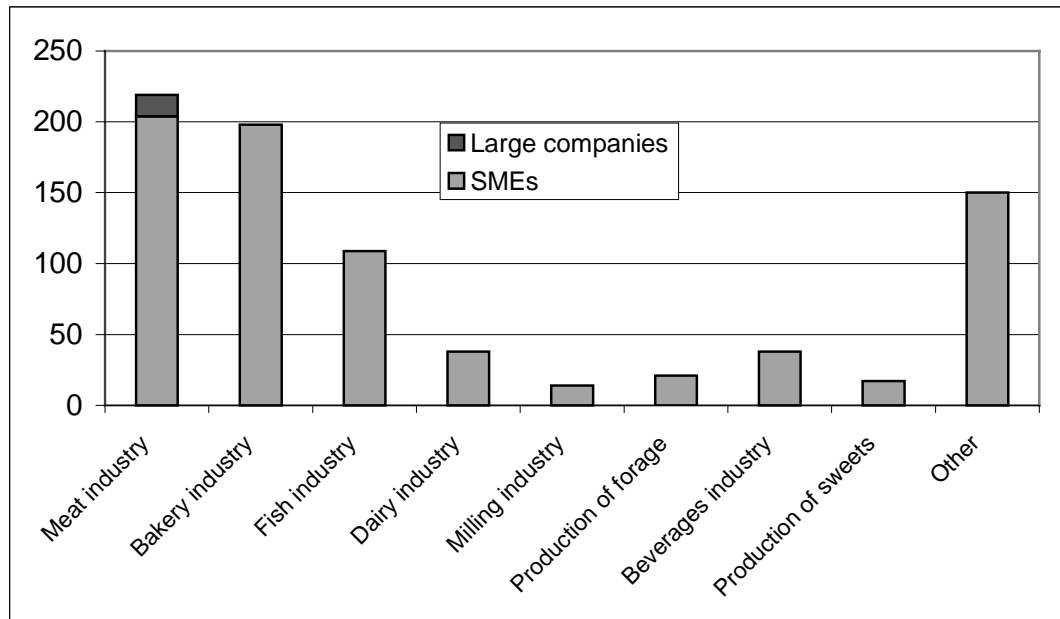
Figure 2.15: Share of food industry in industrial output in %



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 reconstruction 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 where 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 to date (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 (EMA), 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 13<sup>th</sup>, 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 interviewees 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 proteome 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 compartments 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) feeds into biotechnology 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 automatisisation" 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 biotechnology. 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
<b>Scientific performance</b>													
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
<b>Commercial performance</b>													
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 economically 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.

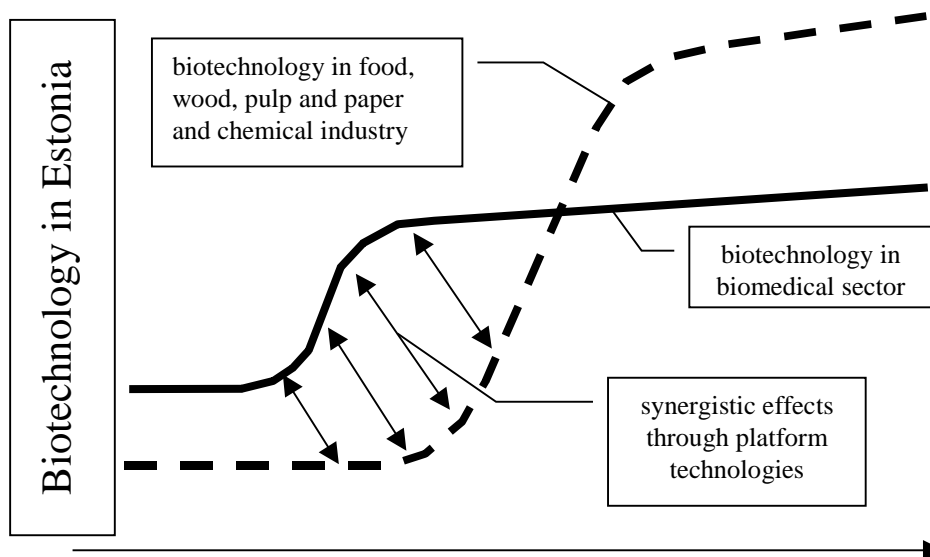
Although it can be expected that dedicated biotechnology companies will grow in the coming years in Estonia, their impact on the national economy in terms of employment, turnover generated and exports will remain limited given their current starting position. In addition it seems unlikely that existing 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 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.

#### **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.
- 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 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 the following table (table 4.1).

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

<b>orientation</b>	<b>essential contents for curricula</b>
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. However, it should be assured that enough money is dedicated to basic research 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<sup>10</sup>, 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.

### **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

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<sup>10</sup> Another specific project dealt with these aspects which was finalized in 2002.

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 includes 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.

### **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 health food products that e. g. provide proven health benefits for elderly people with high blood cholesterol level. The precise definition of the order should be elaborated together with food and health experts. Such an activity would fit well into the portfolio of Enterprise Estonia.

#### **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.

## **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 90 million EEK for five years. About 53 % are planned for interdisciplinary research, 21 % for updating scientific infrastructure, and 26 % 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 food sector.
- 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 350 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
<b>1. Knowledge base</b>		
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	
<b>2. Education</b>		
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
<b>3. Commercial development</b>		
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	