

The industrial use of biobanks in Sweden: an overview

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Introduction

This chapter deals with economic and industrial policy aspects on the use of biobanks in different research contexts.¹ The main question that constitutes the starting point for this study is how different economic interests can be taken account of without coming into conflict with other vital interests held by individuals and the society at large. “Actors” with economic interests are primarily companies within the pharmaceutical, diagnostics and biotechnology industries and those health care and research institutions that administer biobanks. Given the fact that Swedish academic researchers, unlike the situation in many other countries, own the property rights to their inventions, individual scientists might also have economic interests related to biobanks.

Background

The bio industries, dedicated to satisfying the needs of the health care sector for such products as pharmaceuticals, diagnostics and medical devices, are by nature research-based. Their product development is to a large extent based on knowledge generated in research, carried out either in-house or externally by universities, institutes and other companies. By tradition, the bio industries have always been strongly dependent on academic research – preclinical as well as clinical. There are many different ways in which research results can be exploited by companies, including the use of scientific publications, acquisition of patent rights, contract research, recruitment of PhDs, and collaboration between industry and academia.

The pharmaceutical industry, in particular, has a long tradition of commercialising scientific discoveries and inventions. In Sweden, the two leading manufacturers, AstraZeneca and the Pharmacia Corporation (and their predecessors), have longstanding, fruitful co-operation with Swedish academic researchers. This has led to several product innovations that have achieved commercial success in the world market. The co-operation has been both formal and informal. In recent years, research-based biotechnology companies have acquired an important role in the development of new drugs and diagnostics. These companies, many of which are spin-offs from universities, further develop scientific discoveries and product inventions and subsequently sell the results, often in the form of a licence, to large firms. It is the latter who have the resources necessary to complete the product development and bring the final product to the market. In Sweden, a rapidly growing and internationally successful biotechnology industry has emerged during the last 10-15 years. As a rule, these firms have

close contacts with academic researchers in Sweden as well as abroad and offer their services to the international pharmaceutical industry. Besides the typical research companies, the Swedish biotechnology industry includes a number of successful manufacturers of research tools (equipment, chemicals, software...).

Human biological material has long been used in medical research. However, thanks to the great advances in molecular biology and other “modern” disciplines within the life sciences, the need for using cell and tissue samples from human beings has increased dramatically in recent years. In particular, the new knowledge about DNA sequences produced, for example, by the Human Genome Project, constitutes a starting point for intensive research efforts directed at identifying genes and their function. By studying relationships between the DNA sequences in different genes (and their variation among individuals), the molecular and cellular mechanisms in the body, and clinical information about individuals, new knowledge can be gained about the causes of different diseases and their development. In the next step, this knowledge can be used in the development of new diagnostic and therapeutic products. For example, the proteins coded for by identified “disease genes” can be made targets for drug development.

In conclusion, genetic analyses on human cell and tissue material stored in various biobanks will be an important activity in much of the research that follows in the wake of the human genome projects. Therefore, the increasing interest in biobanks demonstrated by both academic and industrial researchers is no surprise. It is a question of using already existing biobanks, which have been created for clinical or research purposes, and building up new biobanks within the frame of specific research projects. As discussed in more detail in other parts of this book, this interest may partly conflict with other vital interests, above all the wish of individual citizens to protect their personal integrity and receive guarantees that sensitive information (e.g., about hereditary disposition for disease) cannot be accessed and improperly used by unauthorised people. Another interest that may possibly come into conflict with commercial exploitation is the need of researchers and health care providers to use the biobanks in their own activities.

The industrial use of biobanks can take place in two different ways. One is for firms themselves to collect samples and build up proprietary biobanks that are used in internal research and development (R&D) projects. The other way is to co-operate with academic researchers or biotechnology firms that have their own biological material, or can get access to such material through a third party. In the latter case, companies can use information extractable from the material without having to build up their own biobanks.

There are several reasons why it is important that industrial firms should be able to utilise efficiently the information that can be gained through research on biobanks. First of all, it is evident that the industry plays an important role in the innovation process whereby research results are transformed into practically useful products that can be made available to the large mass of users and customers in the health care sector. No other actors have the resources and competencies necessary to perform this task. The new scientific advances in biotechnology open the way to completely new methods of diagnosing and treating diseases. In order for humanity to benefit from this progress, companies must be allowed to commercialise this knowledge. This includes the information embedded in the samples stored in biobanks. If the involvement of industry is rendered difficult, for example as a result of excessively rigid regulations, there is a great risk that the scientific discoveries, and the related opportunities to improve health care, will not be used to the best advantage.

Furthermore, from a national perspective there is also an industrial policy argument why it is important that Sweden-based companies are offered good opportunities to use biobanks, either directly or indirectly via co-operation with academic researchers. As explained in other chapters, Sweden seems to provide favourable conditions for conducting

this type of research and development. Thus, if the industry is given the possibility of using, in a reasonable way, the biobanks and related research resources at Swedish universities and health care institutions, this can help to increase corporate development capability and lead to new, innovative products. If in addition these products prove commercially successful, positive effects can be achieved on employment and economic growth.

Purpose and research questions

The overall objective of the project is to create conditions that support an effective and ethical use of Swedish biobanks. Within the frame of this goal the purpose of the present study is to analyse, from an industrial policy perspective, how different interests (economic and others) associated with human biobanks can be balanced. There are several economic and industrial political issues that need to be highlighted in order for us to work out a proposal for legislation and guidelines that take into account the different public, private and commercial interests.

There are at least two types of “actors” that have a direct economic interest in biobanks. First, there are firms that for commercial reasons want to have access to the biological material itself or the information that can be extracted by analysing the samples. Second, the biobanks represent a value to the academic and health care institutions administering them. First of all there is a value linked to the original purpose of collecting and storing the samples. This is normally scientific or clinical. But in both cases there is also a potential economic value, given the fact that others (i.e. researchers or companies) might be interested in using the material, and might be prepared to pay for it, or for the information that can be extracted. The high costs associated with building and managing biobanks constitute another economic aspect.

As mentioned previously, there is a third category of actors that might have an economic interest, namely the academic researchers who make patentable inventions based on biobanks and want to participate in their commercialisation. In this study, however, we have chosen to concentrate on the two first-mentioned types of actors.

As a first step in this study, we need to map the extent to which biobanks are used by Swedish firms.² Some important questions are: Which firms in Sweden actually use biobanks? For what purposes? Have they built up their own biobanks? Which external biobanks do they use? How do they use them? How are the ethical issues handled? What are the results? It is also of interest to find out what kind of plans the companies have in regard to biobanks and related R&D, and furthermore, how they look upon the industrial use of publicly administered biobanks. For example, what problems and opportunities do they see in this connection? What are their opinions on and wishes regarding the coming regulation of biobanks? How does co-operation with universities and health care institutions work?

Other important questions have to do with the effects deriving from industrial use. For example, how can the development and growth of the individual firms, and the industry as a whole, be affected? In what ways can the universities and the health care sector benefit from industrial involvement in biobank-related research?

In addition to the above questions focusing on the companies that use, or plan to use, biobanks, we are also interested in (related) questions pertaining to the administration of public biobanks. In this study, we do not attempt to map the existence of biobanks in Sweden. But we do also want to highlight the commercialisation issue from the viewpoint of the academic researchers and the health care institutions. For example, how are biobanks currently used for research, and in particular industry-related research? What interest has the industry shown in the biobanks and related research activities? How does possible co-

operation with industry proceed? Of special importance in this context is how the ethical problems have been solved.

Furthermore, against the background of the growing interest in using biobanks for various R&D purposes, important questions can be raised regarding the organisation, management and financing of public biobanks. This issue is relevant both for the county councils (i.e., the authority responsible for the health care) and for the universities. Given the value of biobanks for research, their high management costs, and the ethical and legal constraints, to what extent and on what conditions should the samples be made available for external use, e.g., for commercial purposes? How should biobank activities be organised and managed so that the samples can be used by external actors without coming into conflict with other vital interests, such as the protection of personal integrity and the need to use the material for internal purposes?

A short note on the methodology

The first year's work has mainly concentrated on making an overview of the industrial use of Swedish biobanks. Personal interviews, focusing on the questions discussed above, have been carried out with the two large pharmaceutical firms – that is AstraZeneca (or rather its research unit in Mölndal) and Pharmacia & Upjohn (today the Pharmacia Corporation) – and with a number of other firms that were known to use or be interested in using biobanks. These are Amersham Pharmacia Biotech, Arexis, Eurona Medical (today Gemini Genomics), Pharmacia & Upjohn Diagnostics (today Pharmacia Diagnostics), Sangtec Medical and UmanGenomics. In addition, two clinical research organisations (Clinical Data Care and Quintiles) and some of the larger biotechnology firms in Sweden have been interviewed by telephone.

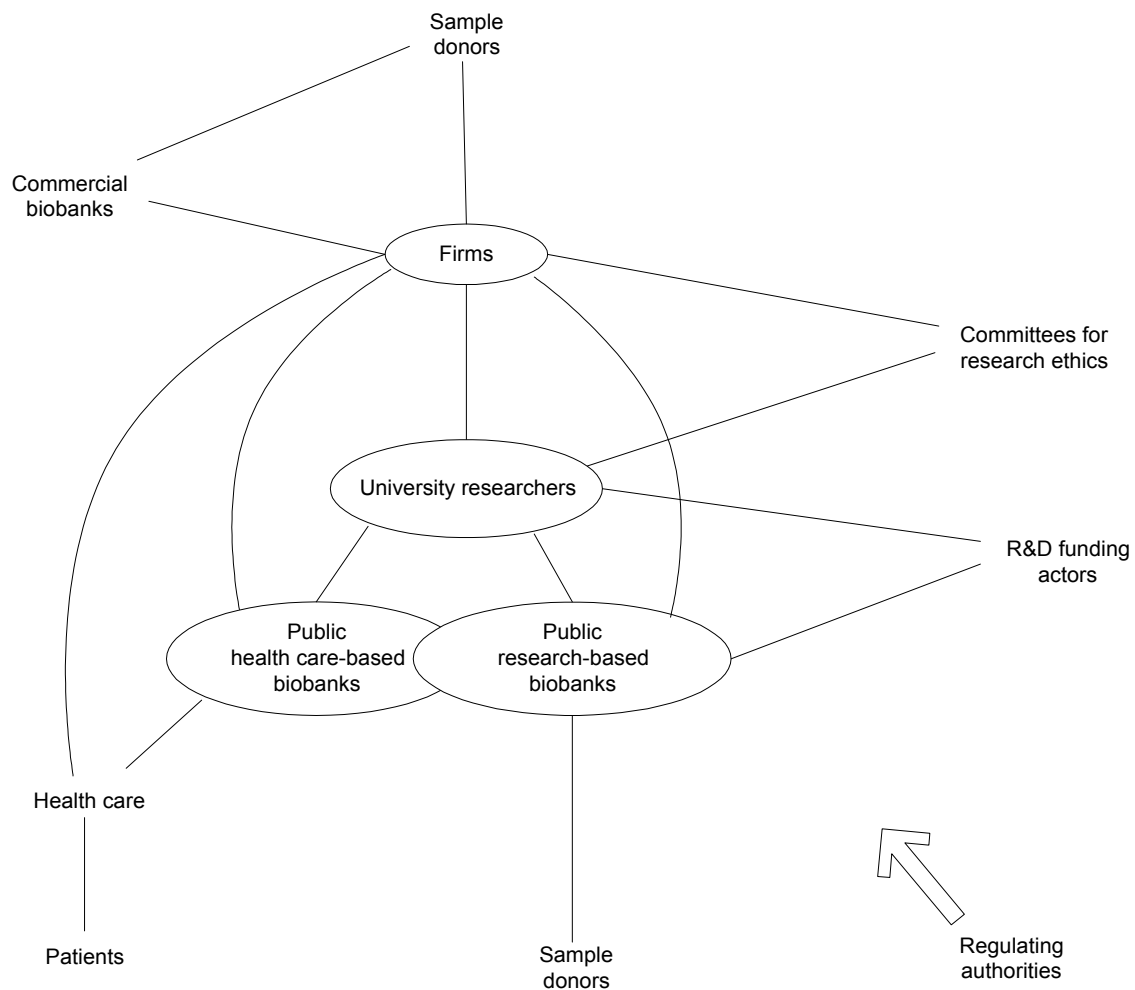
On the biobank side, personal interviews have been carried out with the heads of two pathology departments at university hospitals, and with representatives of three research units that have created biobanks and have had co-operation with industry. These are the so-called Medical Biobank in Umeå, the Swedish Twin Registry at the Karolinska Institute, and the Geriatric Unit at Uppsala University. Finally, interviews have been carried out with a few other people having expert knowledge in fields relevant to the study (e.g., clinical testing).

The names of all the people interviewed personally are listed in Appendix 1. Most of the interviews were conducted during the second half of 1999 and the first half of 2000. However, contacts have also occurred later, for example in order to follow up on the development of the respective company or institution. It can be added that a lot of valuable information has been obtained by other means. For example, the project has arranged several “hearings” with representatives of different interest groups, and the author has participated in several seminars and conferences where biobanks have been discussed.

The biobank actors

To give the reader a feeling for the kind of “environment” in which the industrial use of biobanks takes place, the most important categories of “actors” involved in the creation, management and use of biobanks will be presented in this section. Figure 1 illustrates the current situation, including key relations among the actors. It should be noted, however, that the field is very dynamic, which means that the picture may look different in the future.

Figure 1. Different types of actors involved in biobanks



As a first step, two main types of public biobanks can be distinguished, viz. the health care-based and the research-based. The biobanks can be perceived as “actors” in the sense that there is always some organisation or person who, officially or unofficially, is responsible for the administration of the biobank. The biobank receives samples and connected information either from health care institutions (e.g., the treatment-responsible physician) or directly from the donors themselves, who can be healthy or sick persons.

In Sweden, large health care-based biobanks exist at 35 different pathology departments (altogether approximately 80 million paraffin blocks collected since the 1940s). The material, originally received for diagnostic purposes, is used in research carried out by the pathologists themselves and by researchers from other clinics. Other health care-based sample collections can be found, for example, at the hospital’s blood centres and clinical-chemical laboratories, and at clinics for oncology, immunology and medical genetics.

Within the universities, many research-based biobanks have been created by individual or groups of researchers. In most cases, these collections are study-specific and concern a certain type of disease. In recent years it has become more common to collect and store samples that can be used for DNA analysis, for example in connection with future studies on the importance of hereditary factors. Another type of research-based biobank is “population-based”. This consists of a large sample collection that is representative of a

whole population (i.e., there are no socio-economic differences between those individuals who have donated samples and those who have not). One such biobank investigated in the present study is the Medical Biobank in Umeå. In the southern health care region in Sweden, with 1.5 million inhabitants, it is planned to build up a new biobank consisting of samples from 50,000 randomly chosen citizens. The intention is to use it, for example, in studies comparing susceptibility genes and diseases.

As indicated in figure 1, there is some overlap between the health care- and research-based biobanks. The borderline is not always clear, since for example many research-based biobanks get help from health care personnel with collecting samples. Moreover, physicians working at university hospitals often have dual appointments. In the case of the Medical Biobank in Umeå, the university and the county council have agreed to share responsibility for the biobank. At the University Hospital in Lund there are plans to create a central organisation for all biobanks regardless of origin.³

Beside the public biobanks there are private firms, though not in Sweden, that collect biological material (and some information) from voluntary donors for commercial purposes. Samples coming from these commercial biobanks are then offered for sale to companies.

Needless to say, the university researchers using the biobank constitute a central actor category. As mentioned above, many of them are also involved in the collection of samples. Given the mapping of the human genome, which is almost finished by now, and the consequent opportunities for studying the relations between genetics, environment and disease, biobanks are of potential interest to practically all clinically oriented researchers. We do not know how many researchers in Sweden are actually using biobanks. There is no doubt, however, that genetic analyses are being included in more and more studies. This implies a growing need for co-operation between researchers and health care providers.

There are different kinds of funding actors involved in biobanks. While health care-based biobanks are normally financed internally by the county councils, special funding is in most cases needed in order to build, administer, and use research-based biobanks. In Sweden, experiences show that funding of the research activities, including sample collection, can often be obtained.⁴ But it is more difficult to get funding for the creation, organising and maintenance of the biobanks themselves.

In most countries, Sweden included, all research projects involving human subjects must be evaluated and approved by a local or regional committee for research ethics. These committees influence the conditions for using biobanks (e.g., whether renewed informed consent from the donors is required). In Sweden, the Medical Research Council in 1999 issued new ethical guidelines for biobanks.⁵ These are intended for the research ethics committees as well as individual researchers and companies.

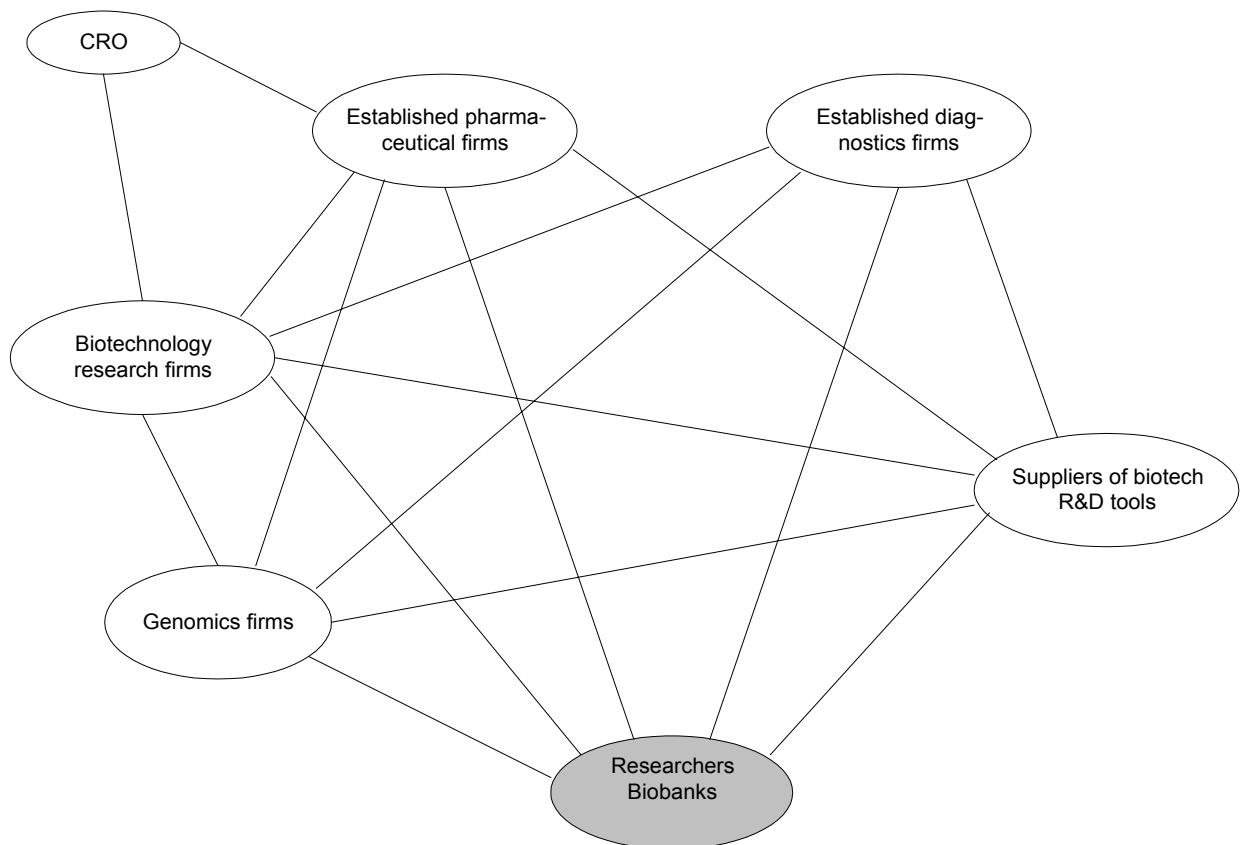
There are, as one can imagine, many regulating authorities that in different ways influence biobank-related activities. In Sweden, two of the most important ones are the National Board of Health and Welfare and the Medical Products Agency. The former is the supervisory authority for the health care sector and by consequence concerned by the activities around the health care-based biobanks. The task of the latter authority is to safeguard the safety and quality of pharmaceutical products. It must give its approval before clinical trials can be carried out. For example, they would not allow collection of biological samples for DNA-testing unless ample justification can be shown for doing so. Sweden has not had any special legislation on biobanks, but in May 2000 the National Board of Health and Welfare submitted a draft bill on the subject.⁶

Given the focus of this chapter on the industrial use of biobanks, the companies constitute key actors in the network of biobank-related exchange relationships that (for analytical purposes) can be defined. The companies carrying out research where biobanks are used can gain access to the material in different ways. They can build up their own collections

by getting samples from health care institutions, directly from individuals, or by purchasing them from commercial biobanks. As we will see later on, though, Swedish firms rarely have their own biobanks. An alternative used by some firms is to get access to biological material via contacts with academic or health care institutions. The predominant pattern, so far at least, is that firms establish research co-operation with academic researchers, who in turn use biobanks in the sponsored studies.

Figure 2 illustrates the most important categories of firms involved in biobanks. They are found within four different industries: pharmaceuticals, diagnostics, biotech, and contract research. The biotechnology industry is not very uniform, but is made up of firms with quite varying operations. Here, three sub-categories have been distinguished. One is research companies using various biotechnological tools. The second sub-category, genomics companies, also have research as their core activity, but due to their focus on genomics we have chosen to separate them here. Suppliers of biotechnological R&D tools make up the third sub-category. Contract research organisations (CRO), that specialise on providing clinical research services, may also be involved in biobanks, for example, if they carry out trials where biological samples are collected for the purpose of DNA testing.

Figure 2. Different categories of firms involved in biobanks



For the last twenty years, the Swedish pharmaceutical industry has been dominated by two companies. They have now merged with foreign corporations and are parts of large international groups, viz. AstraZeneca and the Pharmacia Corporation. Besides these two, there are just a few smaller established pharmaceutical firms. Also the established diagnostics industry is highly concentrated. The dominant manufacturer of immuno-diagnostic products is

Pharmacia Diagnostics (previously Pharmacia & Upjohn Diagnostics). Of special interest from a biobank perspective are companies active in the field of DNA analysis. The undisputed leader here is Sangtec Medical, which already has a commercial product on the market. There are a few others, but they are quite small.

As mentioned in the introductory section, Sweden has a rather successful and rapidly growing biotechnology industry. This includes an increasing number of research companies focusing on drug development.⁷ As elsewhere, many of these companies pursue a strategy, which implies a linking role between the established firms and the academic world. Based on research findings they develop new products, which are sold off, often on a licensing basis, to “big pharma”.

Genomics research is not only carried out by universities and governmental research institutes. Especially in the USA, a number of private genomics companies have been established. The most well-known is Celera Genomics, which, partly in competition with the publicly funded Human Genome Project (HGP), is working on the mapping of the human genome. Most genomics companies, however, concentrate on more applied fields, such as the search for disease or risk genes and the identification of targets for drug and diagnostics development. In Sweden, there are as yet very few companies of this type. One possible explanation, offered by one of our interviewees, is the previous sceptical attitude to gene technology within the research community and the unbalanced ethics debate during the 1980s and 1990s. Eureka Medical, with focus on pharmacogenomics, was the first company to be formed (in 1994). Last year, it was acquired by British Gemini Genomics. In 1999, UmanGenomics was established with the purpose of commercialising the Medical Biobank in Umeå. The exclusive access to this important resource is expected to give this company strong competitive advantages in the world market. Arexis is a newly established biotech company, that specialises in functional genomics.

The last category in figure 2 is the suppliers of biotechnological R&D tools. It is a field where Sweden, thanks to many years of excellent academic research and a small number of innovative firms, holds a leading position. Amersham Pharmacia Biotech (“AP Biotech”) is one of the world’s largest suppliers of products for biochemistry and molecular biology research. Biacore, a leading manufacturer of biosensors, is a spin-off from AP Biotech. PyroSequencing is a new company, which is now commercialising a unique method for DNA sequencing. The technique is especially well suited for analysis of single nucleotide polymorphisms (SNPs) and therefore of great value to applied genomics. There are approximately ten other firms, but they are quite small. Some of them work with bioinformatics. That is an area that has not had a strong position in Sweden. Current investments in bioinformatics research aim to change this.

Finally, it should be emphasised that the bio industries are strongly international. It means, for example, that even the small firms go international early. The high degree of internationalisation is also reflected by the fact that many of the Sweden-based firms have foreign owners. This holds not only for the large corporations, but also for many of the small ones.

Some biobanks and their industrial contacts

The ethics debate on biobanks has to a large extent focused on the so-called pathology archives. The reason is probably that these tissue banks contain very large amounts of samples, which in addition have been collected and stored for health care purposes. Now, there is increasing interest in using them for a different purpose – research. Most of the

donors are unaware that the samples might be used in research, and that there might even be commercial interests involved.

By tradition, the pathologists have assumed that they have the right of disposal of the samples stored in their archives. When it comes to the question of ownership, though, the situation has been perceived to be unclear. It seems that the ongoing ethics debate has contributed to increase the uncertainty around biobanks.⁸

Within both of the pathology departments investigated, human tissue is often used in research projects. Some of the projects are in-house, others are carried out in co-operation with other researchers at the same hospital or other Swedish hospitals. In some projects, the pathologists collaborate with molecular geneticists. It is estimated that today DNA analyses are used in more than half of the studies. So far, the industry has shown limited interest in the biobanks. A few years ago, The Uppsala University Hospital co-operated with Eureka Medical. However, the company came to the conclusion that the pathology archives were of no great use to them. They preferred using study-specific research-based biobanks, one of the advantages being that the material is better characterised. Both departments have collaborated with AP Biotech. Some years ago, this company was developing molecular biological methods for tumour screening. As one type of activity, a number of collaborative studies were carried out together with clinical research groups in Sweden and abroad. The samples were sent, in coded form, to AP Biotech, which performed the genetic analyses in its own laboratories. The results were subsequently transferred to and used by the academic partners.

One of the physicists interviewed believes that the pathology archives have a limited commercial value, the reason being that they are too fragmented (few samples and patients for each disease) and that the samples and the information have not been collected in a systematic way (compare Eureka). AP Biotech, however, say they have obtained useful knowledge through the above-mentioned studies. Given their focus on cancer, major cost and time savings can be achieved by conducting retrospective studies where existing biobanks are used. They see the public biobanks as an important national resource that should be made available for research and industrial development.

Some brief information on the three investigated research-based biobanks will now be given.⁹ Let us start with the Medical Biobank in Umeå. It was in the mid-1980s that researchers at Umeå University began to build up this biobank in co-operation with the county council in Västerbotten (in connection to health screenings). The biobank is population-based and currently consists of some 105,000 blood samples from approximately 80,000 individuals. For each donor there is also clinical and other information.

Since the beginning, each individual has been asked to sign a donation form, which says that the sample is donated for “future disease-preventing research”. Today, the existence of this written consent is seen as a very important asset, since it facilitates the use of the samples for research. In the mid-1990s, the idea to commercialise the biobank began to take shape. At first, there were plans to establish joint ventures with large industrial firms. There were some discussions with AP Biotech, but the idea of creating a joint “service unit” for carrying out contract research did not materialise. Instead, the university and the county council decided to establish UmanGenomics AB (February 1999). This company has been granted the exclusive right to commercialise the knowledge about disease-related genes and genetic and biochemical markers that can be gained by using the samples and associated information. The agreements made among the different parties do not impede academic researchers from using the material, but other companies cannot get access to the biobank unless UmanGenomics gives its consent.

UmanGenomics has recently started up its operations and got its first customers. The samples and the information are transferred to the company in coded form and only after

approval by the research ethics committee. The analysis results are fed back to the Medical Biobank, which after a reorganisation is now part of the county's health care organisation.

ULSAM is a longitudinal study on mortality in different age-related diseases, which in the 1970s was started by Uppsala University's unit for geriatric research. When the cohort (2,300 subjects) was examined for the third time around 1990, samples for DNA analysis were collected. Some years later, the existence of this biobank drew the attention of Eurona. As a result, a research co-operation on the regulation of cardiovascular diseases was initiated. Eurona saw a potential in using the biobank, and related information and research competence, in its development of pharmacogenomic tests. A first product has been developed, but it has not been launched into the market due to Gemini Genomics' acquisition of Eurona.

The DNA analyses have been carried out by Eurona, which also has been entrusted with storing the samples in its premises. The reason given for this was that the company had better resources and systems. All samples and information have been coded, and the code key has been kept at the university.

According to the research leader at the university, the advantage of co-operating with the industry is that the company can add valuable resources. The main disadvantage is that the publication of the research findings may be delayed due to the patenting process. Another complication, illustrated by the Eurona case, is that strategic changes in the company can have negative effects on the project.

The Swedish Twin Registry, administered by the Karolinska Institute, dates back to the 1960s. Today, it contains data from more than 140,000 twins, which makes it the world's largest. The registry is used for research on the relative importance of heredity and environment. The data collection is carried out both continuously and project-wise. Biological samples have been saved since the mid-1980s. Owing, however, to funding constraints large-scale and systematic collection and storage of samples has yet to be realised.

The first industrial co-operation took place in 1996-97. Astra and Pharmacia & Upjohn financed a pilot study for a large screening project (some 60,000 subjects). Besides the interview data, blood samples were collected for genetic analysis. The main study is now ongoing, with public funding. The Twin Registry, however, has failed to get money for the biobanking activities. Later on, consequently, the researchers will have to get back to the twins and ask for samples.¹⁰

Both Astra and Pharmacia & Upjohn have shown interest in continuing the co-operation and support the registry in its attempts to get funding for the bigger biobank. At present, the level of activity is relatively low, probably as a consequence of the merger processes that both companies are involved in. The Twin Registry has been in contact with some other companies, which are interested in getting access to information. They are now waiting for the results of the screening study.

The use of biobanks in Swedish industry

As already hinted, the industrial use of biobanks in Sweden is so far quite limited. There are only a few companies that actually use biobanks and in most cases it is only done on a small scale. Some other companies have plans to start up research activities.

Table 1 shows with which companies personal interviews have been carried out. Apart from these, four other biotechnology firms (Active Biotech, Karo Bio, Medivir, and PyroSequencing) were interviewed by telephone. None of them have used biological samples of the kind dealt with in our study. A couple of them believe that they will use biobanks in the future and that, probably, it will take place in co-operation with universities. There are more

than hundred other biotech firms in Sweden. The possibility of some of them having used or planning to use biobanks cannot be excluded, but in the course of our study we have not come across any information of this kind.

Table 1. Swedish firms that are using or planning to use biobanks

Company	Category	Has already used Swedish biobanks	Is planning to use Swedish biobanks
AstraZeneca (Mölndal)	Pharmaceutical firm	yes	
Pharmacia & Upjohn	Pharmaceutical firm	yes	
Pharmacia & Upjohn Diagnostics	Diagnostics firm	(yes)*	
Sangtec Medical	Diagnostics firm	no	Yes
Arexis	Biotech firm	no	Yes
Eurona Medical/ Gemini Genomics	Genomics firm	yes	
UmanGenomics	Genomics firm	yes	
Amersham Pharmacia Biotech	Supplier of biotech R&D tools	yes	

* The biobank consists of blood serum only.

The use of external biobanks

With one exception, Pharmacia Diagnostics (with a collection of serum samples which cannot be used for DNA analysis), the companies investigated have not invested any resources in building up their own biobanks. Instead, the dominant pattern so far is co-operation with academic researchers. The latter have relevant research questions. They also have access to existing biobanks or can collect samples. The pharmaceutical firms have used biobanks primarily in exploratory research projects, for example with the aim of finding susceptibility genes and identifying drug targets. Most commonly, as it seems, the practical work is carried out by the academics. The sponsoring company is only interested in gaining access to the results and being able to make patent applications on possible inventions. There are other cases where the company not only formulates the questions but also carries out the research, with the help of samples received from the university. One of the companies says that in future they might be interested in also purchasing samples from commercial biobanks. In such a case, there would be no uncertainty with regard to ownership.

Outside Sweden as well, co-operation with the academic world seems to be the dominant mode in the pharmaceutical industry. There are, however, a few large companies – such as Roche, SmithKline Beecham and Glaxo Wellcome.¹¹ – which have built up their own biobanks. Some others, e.g. Pharmacia, have samples that they have collected in connection to clinical trials. In future, this material might be used for genetic analysis. It can also be mentioned that recently AstraZeneca in Sweden has begun to bank some tissue samples – so far, though, on a very limited scale.¹²

Besides the academic co-operation it is not unusual for pharmaceutical firms to buy R&D services from genomics companies. Pharmacia, for example, has linked up with Celera Genomics and Exelixis Pharmaceuticals in the USA and with Genset in France. AstraZeneca has made agreements with Millennium Pharmaceuticals in the USA and Oxagen in the UK. This last-mentioned co-operation is aimed at identifying the underlying causes of arteriosclerosis.¹³

Besides the drug discovery phase, pharmaceutical firms may also use biological samples for DNA analysis in clinical trials, e.g. for the purpose of identifying “genetic signatures” related to a drug’s effectiveness or side-effects. Up till now, pharmacogenomic studies of this kind have been rare (approximately one per cent of all clinical trials world wide, at one interviewee’s estimate). That the industry’s interest in genotyping patients in connection to clinical trials is rapidly increasing was shown by a study presented in the USA a couple of years ago.¹⁴ This picture tallies with the information we have obtained about Sweden. Nowadays, it is not uncommon for industrial researchers to want to take “an extra tube with blood” for future DNA analysis. That is not allowed by the Medical Products Agency, however, unless the company can give a good reason why the sample should be taken. None of the two CROs have been involved in building biobanks for the pharmaceutical industry in Sweden. One of them has good hopes that in the future such assignments will come, especially from biotech firms.

Sangtec Medical and AP Biotech are both interested in molecular diagnostics. Like the pharmaceutical firms they have chosen to co-operate with academia. As already mentioned, AP Biotech has carried out a number of studies with university groups in several European countries. Sangtec has established contacts with several Swedish groups, but the actual work has not yet started, since they are waiting for the regulatory situation to become clearer.

The genomics companies are in a somewhat different situation than the previous categories. Both Eurona Medical/Gemini Genomics and UmanGenomics are among those firms whose business idea is to sell information based on studies of human biological material (many genomics companies use model organisms). Accordingly, they need samples that they can work with in their own laboratories. Eurona has gained access to samples through co-operation with researchers at several Swedish universities. As mentioned already, UmanGenomics has access to samples stored at the Medical Biobank in Umeå.

Even if it is true that the actual use of biobanks for commercial purposes is still limited, the interviewees agree that biobanks will be increasingly used in the genomics and medical research following on the human genome projects. Regardless of whether the applied research is carried out in academia or industry, the outcome will provide the basis for developing new therapeutic and diagnostic products. Also when it comes to clinical trials, it can be expected that genetic analyses and biobanking will become more common.

Type of biobank

In most industry-related projects, existing research-based biobanks are used. They can be either disease-specific or population-based. The latter category is of particular value in the kind of hypothesis-testing studies where there is a need for large numbers of samples in order to verify suspected relations between genotype and phenotype.

Thus, health care-based biobanks have not been used to such a very great extent. There are several reasons for this, as has already been remarked. Collection has not been systematically and uniformly carried out, which reduces their usefulness in many of the studies that the industry is interested in. Moreover, the pathology archives are mainly cancer-based and therefore of interest mainly for companies working in that particular field (such as Sangtec and AP Biotech).

Swedish vs. foreign biobanks

The international character of the bio industries leaves its mark also on the use of biobanks. The large companies, i.e. AstraZeneca, Pharmacia, and AP Biotech, all have, or have had, biobank-based co-operation both in Sweden and abroad. Sangtec plans to establish co-operation with Swedish universities, but if the regulatory issues are not satisfactorily solved, going abroad is seen as a feasible alternative. The two genomics companies are more locally anchored. It is part of their business ideas to commercialise Swedish biobanks. It can be noted that the newly started Arexis has established its first biobank-related co-operation with an Italian university.

All the industrial representatives maintain that there are important advantages associated with carrying out biobank-related research in Sweden. The main arguments build on the availability of high-quality collections of biological samples, the excellent possibilities to get clinical information about the donors, the high epidemiological competence, and the fact that Swedes in general tend to trust the health care system, the authorities and the medical community. Thus, it is not only a matter of using existing biobanks. More important, perhaps, are the general characteristics of the Swedish health care and medical research systems, which facilitate clinically oriented research. This might give Sweden a chance to build up a strong position in the area of applied genomics. It is widely believed that if this happens and the impending legislation on biobanks is not too restrictive, there will be positive effects on the development of Swedish industry. Likewise, foreign companies can be attracted to establish co-operation with Swedish academic researchers. Whether this will also lead to foreign investments in local industrial R&D activities, is an open question. For example, there are people at Pharmacia who maintain that effective co-operation can be well achieved without local presence.

Another common opinion is that Sweden needs to substantially expand its research on applied genomics, if the country is to take advantage of the favourable conditions mentioned above. Given the large sums spent on genomics in other countries, especially in the USA, there is otherwise a risk that Sweden instead will lose ground, it is said. This concern may prove to be unjustified. The Swedish government and private foundations have recently decided to support major research programmes aiming at building up functional genomics research at several universities.¹⁵

The possibility of buying samples

In countries such as England, Scotland, Italy and the USA, samples can be purchased from commercial biobanks. In general, this is not considered to be a good alternative by Swedish firms, mainly because the clinical information is insufficient. The buyer may, for example, get information on what disease the donor is suffering from, but not how the patient has been treated and the results. The samples offered for sale may also vary a good deal in quality. The advantage, as perceived at least by one company, is that there is no problem of ownership.

Some viewpoints on the ethical issues

A majority of the interviewees, both from the industry and the universities, express dissatisfaction with the current uncertainty regarding the ethical rules and legislation. They would like to see a clear and national regulation that is equal for companies and academic researchers. Some feel that a new regulation is urgently needed, while others say that they can go on living with today's de facto rules. There is widespread concern that the coming regulation will be too detailed and may therefore soon become outdated. Given the rapidity of

technological changes and the tendency of ethical opinions to evolve over time, broad recommendations or guidelines are called for, based on fundamental and stable ethical judgements.

What many interviewees are particularly concerned about is that the demands on renewed informed consent, when stored samples are used in new studies, will be too far-reaching. If, when the sample is taken, its intended use has to be specified too narrowly, this will be perceived as very troublesome and as a barrier to effective research.

The current system of committees on research ethics is perceived to be a good one. But there seems to be a need for educating the members in the fields of gene technology and genomics. With better-trained committee members, the discussions could to a larger extent be based on grounds of fact, it is said. Among certain industrial representatives there is a suspicion that a “double standard” is applied by the committees, i.e. that the requirements for industrial projects are higher than for pure academic projects.

The company interviewees also tend to believe that the ethical problems are taken less seriously by universities and hospitals than in industry. It could be, for instance, that samples are used for research purposes without consent from the patients or without coding the information. Industrial representatives also maintain that many within the public sector are not fully aware of the strict standards and rules that are applied to industrial R&D (such as, e.g., the international rules for Good Clinical Practice).

As an illustration, it can be mentioned that AstraZeneca has formulated a special policy for handling the ethical issues related to biobanks. It can be summarised as follows: (1) informed consent should always be asked for when the samples are taken, (2) there should always be an approval from the research ethics committee, and (3) the company employees should never get any information about the identity of the donors. It is believed that most other pharmaceutical firms have adopted similar policies.

Another standpoint that has come up in many interviews is that the ethics debate on biobanks has been characterised by a great deal of ignorance. For example, it has sometimes been suggested that transfer of samples to other countries should be prohibited. Such a rule would not only prevent the use of scale-advantages, it would also to a large extent be inoperative, since what matters is the information, and that can easily be transmitted, e.g. by the Internet. Furthermore, the debate has focused too much on DNA testing. In many cases, protein analysis can yield similar information on heredity.

To conclude, our interview data indicate that the enactment of a bill that renders the use of biobanks for research too difficult might have negative effects on the possibilities of carrying out applied genomics research in Sweden. This would not only affect the scientific production (and possibly the development of medicine) but also influence the companies' location of R&D activities. The latter is illustrated by the Sangtec case. Unless the present regulatory uncertainty is solved in a satisfactory manner, the company will start searching for academic partners abroad. As a consequence, future product development and manufacturing activities may also end up in a foreign country.

Concluding remarks and plans for continued research

Without any doubt, biobanks and other human biological materials will become increasingly important for medical research. For example, the new knowledge about disease mechanisms generated by molecular genetics and molecular epidemiology will provide opportunities to develop new products for diagnosis and treatment. In other words, much of the product development in these areas will take its starting point in biobank-based research. A large part of this research will be carried out at academic institutions. It is a fact that more and more,

clinically oriented researchers are focusing their interest on the importance of genetic factors. But, as a result of the industrial relevance of this research, and the high costs involved, it can be expected that an increasing share of the applied genomics and proteomics research will be carried out in industrial laboratories. During the last five years, molecular biology and genomics have come to play an increasingly important role above all in the pharmaceutical industry's exploratory research phase. The aim is to identify biological targets and substances that bind to these targets.

Thus, many of the large pharmaceutical firms have added resources for genomics, bioinformatics and other new biotechnological platforms to their organisations for pre-clinical research. At the same time, however, there is a trend towards "outsourcing" of the exploratory research. It means increasing co-operation both with universities and biotechnology firms. The latter especially have come to play a key role in modern drug development. In the USA, but in Europe too, there are several leading biotechnology firms that have built up considerable resources for genomics and proteomics. This is a very expensive activity, which, coupled with the high commercial potential and the abundance of venture capital, is probably one of the reasons why this research is to such a high degree being carried out by industry.

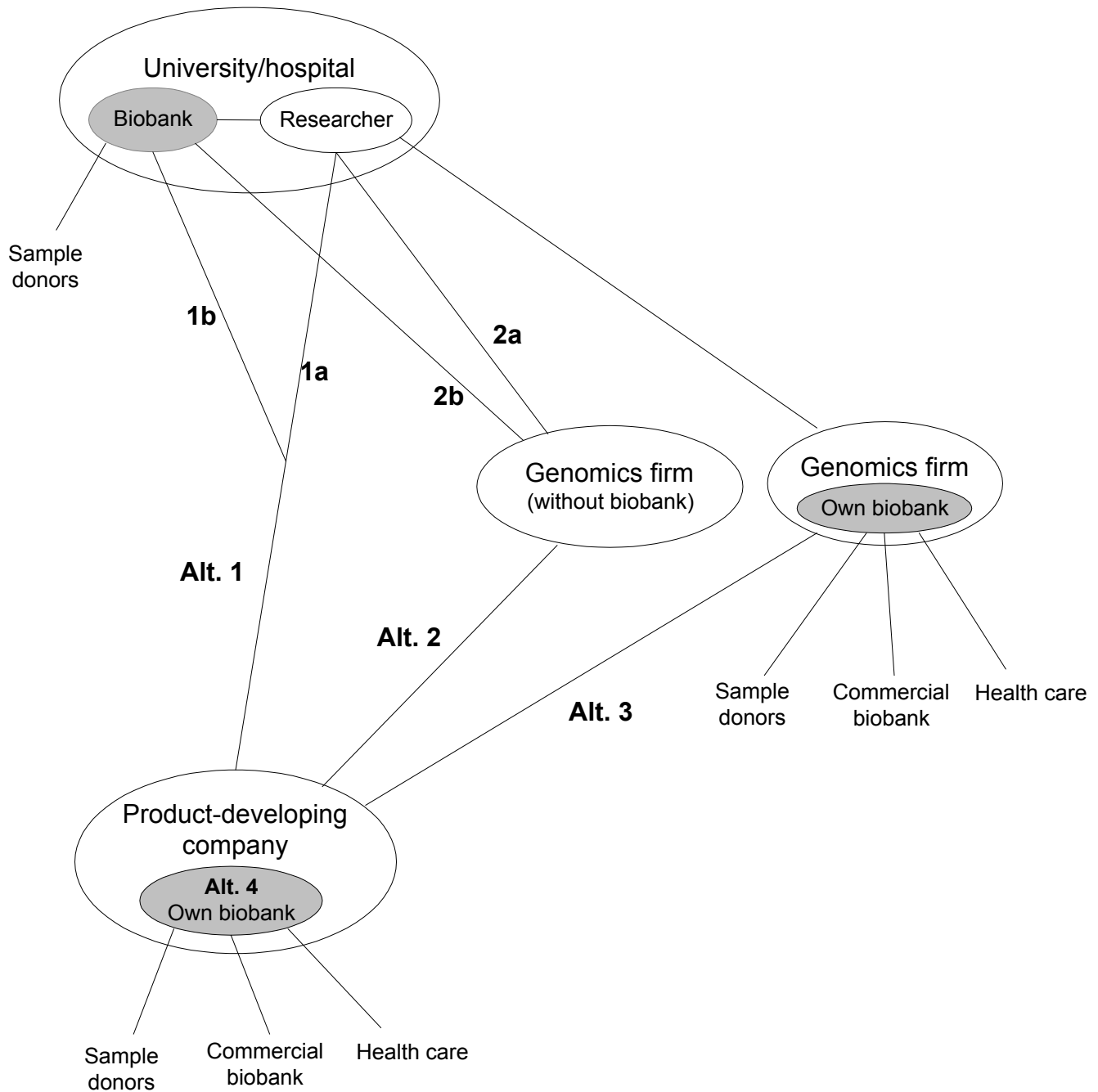
Unfortunately, Sweden is lagging behind in this development. It is true that AstraZeneca and Pharmacia have incorporated molecular biology in their R&D strategies, and there are several successful drug research biotech firms in Sweden, but the genomics industry has been almost non-existent. There is today an embryo consisting of Gemini Genomics, UmanGenomics, Arexis and maybe a few others. On the diagnostics side, there is Sangtec Medical.

We have also seen that Sweden offers favourable conditions for conducting the type of medical research where biobanks are used. The advantages are the existence of high-quality biobanks and, above all, the entire complex consisting of the health care system, the research tradition, the national registration numbers etc., that facilitate the research activities. From an industrial policy point of view, an important question is how Sweden as a nation can exploit these advantages. How should the relevant research investments be realised? And how should the findings be applied to industrial R&D and transformed into commercial products? The latter is, normally, a prerequisite if the results are going to benefit the public. If, furthermore, Swedish firms take care of the commercialisation, there will be positive effects on the industrial and economic development. Obviously, biotechnology is a key industry for the future. In a long-term perspective, it is therefore important that Sweden, as an advanced industrial nation, should succeed in creating an internationally competitive biotech industry. The industrial use of biobanks can be one of several means to such an end.

The first phase of the present study has involved a broad survey of the industrial use of biobanks. In the next phase, the main focus will be on the forms of the industry's involvement in and exploitation of public biobanks. A number of important questions can be identified, such as: Which forms of co-operation between industry and health care/universities exist? What are the pros and cons from the different parties' perspectives? What specific solutions for handling the ethical and legal aspects exist, or can be developed? How should the regulatory system be designed so that it does not bring about unnecessary barriers to effective forms of co-operation? How should the biobank activities be organised at hospitals and universities in order to facilitate co-operation with industry, without causing undesired consequences that cannot be accepted by individual subjects or the society?

These questions will provide important starting points, when in the next phase some specific cases will be more thoroughly investigated. The focus will thus be on the organising of the industrial use of biobanks. The main alternatives are illustrated in figure 3.

Figure 3. Different ways of commercialising biobanks



Alternative 1 is the traditional, direct co-operation between a product-developing company, e.g. a pharmaceutical firm, and a university department or hospital. As we have seen, the typical pattern in Sweden is that it is the academic researchers who have the samples, perform most of the work, and subsequently share the results with the sponsoring company (alt. 1a). In some cases, it is the latter that carries out the DNA analysis. Alternative 1b is a variant where the company, within the frame of a co-operative agreement, gets access to samples, which are subsequently used in the company's internal R&D activities.

Some of the genomics firms act as some form of middleman/intermediary between the established industry and the public sector. Eurona/Gemini and Arexis represent alternative 2a,

i.e., the company gets access to biobank-based research results and/or samples through co-operation with academic researchers. These resources are further refined and then sold to the pharmaceutical and diagnostics industry. UmanGenomics pursues the same strategy within the area of rare, hereditary diseases. But with its core business, on common diseases, UmanGenomics illustrates alternative 2b. It means that the genomics company gets access to samples that are used internally without the academic researchers being directly involved. Thus, when UmanGenomics gets research assignments from its customers, samples obtained from the Medical Biobank are used to carry out the work. The Icelandic deCode Genetics and Oxagen Ltd in the UK are two other genomics companies commercialising information and samples coming from the public sector. The former was established in 1996, through a private initiative, to exploit genetic, clinical and genealogical data about the relatively homogeneous Icelandic population. The latter is a spin-off from Oxford University. It receives samples through co-operation with scientists from different universities in the UK and on the continent.¹⁶

There are also, as illustrated by alternative 3, genomics companies with biobanks of their own. One possibility is to get samples directly from sick or healthy individuals. DNA Sciences is an example from the USA. It uses the Internet to recruit donors (www.dna.com).¹⁷ Other options are to buy samples from commercial biobanks or get them from hospitals. Also in the USA, Ardais Corporation, specialising in clinical genomics, has made agreements with leading medical institutions that will enable them to collect, process and utilise clinical samples that would otherwise be discarded as waste¹⁸. According to what we have heard recently from people in the business, however, the company will be abandoning this approach to sample collection.

The fourth alternative is that the product-developing companies, like in the previous case, build up in-house biobanks. Some of the large pharmaceutical firms have done this, although not in Sweden so far (other than on a very small scale).

As this discussion has shown, the use of biobanks for industrial purposes can take place in a variety of ways. It can be assumed that the different alternatives have different advantages and disadvantages as seen from the different interested parties' point of view. For the present project it would be of great value if we could obtain a better understanding of the various commercialisation forms. Alternative 2 above is of particular interest to us. Judging by initiatives already taken and the ongoing discussion in industry and academia, this type of indirect co-operation between the public sector and the established industry seems to emerge as an important complement to (or sometimes substitute for) the traditional, direct co-operation. It might be that the creation of one or several internationally strong genomics companies is a prerequisite for a successful commercialisation of Swedish biobanks and related research.

The ongoing development in Umeå around the Medical Biobank and UmanGenomics is an interesting case that we intend to investigate further. In fact, several of the interviewees have pointed to UmanGenomics as a possible role model for other parts of Sweden. But there are also those who call into question if the resource base in Umeå is sufficient to achieve international competitiveness. Instead, they call for a more large-scale investment, for example on a nation-wide level.¹⁹ Nevertheless, UmanGenomics provides a good opportunity to study the commercialisation of a public biobank through the establishment of a dedicated genomics firm. Also outside Sweden, genomics companies have been founded for similar purposes. deCode Genetics and Oxagen have already been mentioned. Since the business models as well as the environmental conditions may differ, we believe that it would be fruitful to compare these two ventures with UmanGenomics.

References:

¹ This chapter is a shortened version of a more extensive report in Swedish (Laage-Hellman, J., *Kommersialisering av svenska biobanker: ett näringspolitiskt perspektiv* IMIT-report, Institute for Management of Innovation and Technology, 2001, forthcoming).

² By “Swedish firms” we mean companies carrying on R&D and/or production activities in Sweden. They can be partly or wholly owned by foreign corporations. In fact, a growing proportion of Sweden-based biomedical companies belong to foreign industrial groups.

³ *Biobank vid Universitetssjukhuset i Lund*, The University Hospital in Lund, 1999.

⁴ For example, from various governmental research-funding organisations (such as the present Science Council and VINNOVA), various private foundations, foreign research granting authorities and industry.

⁵ *Forskningsetiska riktlinjer för nyttjande av biobanker, särskilt projekt innefattande genomforskning*, Medical Research Council, 1999.

⁶ The legal aspects of biobanks are dealt with in other chapters of this book.

⁷ According to a report from NUTEK (i.e., the Swedish Board for Technical and Industrial Development) there were in 1998 some forty companies of this kind. Some of them, such as Active Biotech, Biora, Karo Bio, Medivir and Q-Med, were relatively large (more than 40 employees). (Backlund, A., Markusson, N., Norgren, L. och Sandström, A. *Det svenska biotekniska innovationssystemet: drivkrafter och hinder för innovationer och tillväxt* arbetsrapport, NUTEK, 2000.)

⁸ The issue of who possibly owns or has the right of disposal of the biobanks is thoroughly dealt with in the chapter written by Li Westerlund and Annina H. Persson.

⁹ These biobanks are described in more detail in the more lengthy report in Swedish (see note 1).

¹⁰ In 2000, the Swedish Twin Registry was scientifically evaluated. One of the conclusions was that the biobank activities were important and should receive long-term support by establishment of a central facility for handling and storing of samples. (*Scientific Evaluation of the Swedish Twin Registry* FRN-Report 2000:10, Swedish Council for Planning and Coordination of Research, 2000.)

¹¹ The two last mentioned have now merged to form GlaxoSmithKline.

¹² Personal information from Professor Maria Anvret, Director of Molecular Sciences, AstraZeneca R&D Södertälje.

¹³ Astra’s annual report for 1998, p. 30.

¹⁴ Silber, M. *Importance of Pharmacogenomics – Response to 1998 Survey* Paper presented at the conference Pharmacogenomics – commercial developments and practical applications in Philadelphia August 1998.

¹⁵ For example, a 5-year national programme in functional genomics has been granted MSEK 800 by the Knut and Alice Wallenberg Foundation. At the same time, the government is expected to spend SEK 1.1 billion during three years. (See, e.g., *Historisk satsning på forskning Svenska Dagbladet*, 27 March, 2000.)

¹⁶ In the USA, Framingham Genomic Medicine was formed last year to commercialise data from the famous Framingham Heart Study in Massachusetts. However, the company will be disbanded since Boston University and other funding organisations for ethical reasons decided to not grant the company access to the data (Genomics company formed from Framingham heart study *Nature Biotechnology*. Vol. 18, August 2000, p. 818, and *Framingham Genomic Medicine to Disband after Denial of Heart Data* article published 29 December, 2000 on the site <http://www.genomeweb.com/articles>).

¹⁷ DNA Donation Site Draws a Crowd *Science*, Vol. 290, 6 October 2000, p. 7.

¹⁸ Teaching hospitals to share tissue with industry *Nature Medicine*, Vol. 6, No. 10, October 2000, p. 1072; *Ardais Corporation and Leading Medical Centers Launch Initiative to Accelerate Genomics-Based Drug Discovery* (<http://www.fkpi.com/Releases/Ardais>, 9 September 2000).

¹⁹ As described in more detail in the Swedish report (see note 1), a group of Swedish business people has presented a proposal for a national structure for commercialising Swedish tissue banks. The idea is to create a company, Svenska Vävnadsprover AB, that will build up a big, centralised database with genetic and clinical information. Another company, GenostiX AB, will get exclusive rights to commercialise the information by selling analytical services to the pharmaceutical and diagnostics industry.

Appendix 1. Personal interviews

Industry:

Per-Gunnar Bengtsson, head of the biobank, Pharmacia & Upjohn Diagnostics

Jan Brundell, Deputy Managing Director, Sangtec Medical

Mats Inganäs, staff scientist, Amersham Pharmacia Biotech

Ann-Cathrine Jönsson-Rylander, Associate Director Cell Biology and Biochemistry,
AstraZeneca R&D Mölndal

Johan Kördel, project Portfolio Director Metabolic Diseases Research, Pharmacia & Upjohn

Gunnar Olsson, Director Cardiovascular Management & Strategies Clinical R&D,
AstraZeneca

R&D Mölndal

Sune Rosell, Managing Director, UmanGenomics

Torbjörn Schröder, Deputy Managing Director, Eurona Medical

Vidar Wendel-Hansen, Managing Director, Arexis

Universities/health care institutions:

Gunnar Bjursell, Professor of Molecular Biology, Gothenburg University

Nils Conradi, Head of the Department of Pathology, Sahlgrenska University Hospital

Göran Hallmans, Professor of Nutrition Research at Umeå University and head of the the
Medical Biobank, County of Västerbotten

Gerd Johansson, responsible for quality and information, the Medical Biobank, County of
Västerbotten

Hans Lithell, Professor of Geriatrics, Uppsala University

Stefan Lohmander, Professor of Orthopaedics, Lund University

Nancy Pedersen, Professor of Medical Epidemiology and head of the Swedish Twin Registry,
Karolinska Institute.

Christer Sundström, Head of the Department of Pathology, The Uppsala University Hospital.

Others:

Torbjörn L. Möller, consultant, Five plus Five Management

Berit Westberg, consultant (formerly of AstraZeneca, Mölndal)