



ESTONIAN GENOME PROJECT



estonian genome project

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ESTONIAN GENOME PROJECT

The map of the human genome is about to be unraveled. The complete sequence of the human genome is due to be published in 2003. By itself, this knowledge is of limited value and the importance of this discovery will only reach its full potential if this sequence data is explored along with detailed knowledge about health history, genetic profile and genealogy.

Virtually every human trait or disease is the result of complex interactions between genetic factors and the environment. Interactions between and within genetic pathways radiate through an environmental lens to project unique images of individuality. They create biological effects whose magnitude cannot be predicted by having an understanding of the interacting components on their own. In other words, to understand how genetic information contributes to disease, it is necessary to recognize that the whole (the disease or phenotype) is often times greater than the sum of its parts (the genes).

The idea of a national gene bank - Estonian Genome Project - was proposed by Andres Metspalu, a professor of biotechnology at the University of Tartu. Regarding the fact that Estonians are a representative droplet from the European gene pool, the idea had two goals. First, to identify disease genes by comparing genotypes within a group of patients with a given disease. Second, to set up a health care database that would give Estonians access to their own data, so they can benefit from the personalized medicine of the future.

The project was first presented to politicians and the public in 1999 and was developed by a group of scientists under the supervision of the Estonian Genome Foundation (EGF), a non-profit body founded in January 1999 by Estonian scientists, doctors, and politicians to support genetic research and biotechnology in Estonia.

Planning of the Estonian Genome Project began in March 1999 with an agreement between the Estonian government and the EGF. Just days before the announcement of the newly decoded human genome in June 2000 a draft project was submitted to the Estonian Ministry of Social Affairs.

The next step was to establish a legal framework that was considered to be a prerequisite for such a large scale innovative project that involves the majority of the population. It was also agreed that the project must

be carried out by a government-backed structure and regarding a set of principles based on the European consensus to avoid fragmentation of societal solidarity and ensure public acceptability and respectability.

The Human Genes Research Act was prepared by an international working group and guidance was obtained from all available international documents dealing with genetic research, such as the UNESCO Universal Declaration on the Human Genome and Human Rights (1997) and the Council of Europe's Convention on Human Rights and Biomedicine (1997). A unique piece of legislation - Human Genes Research Act - was passed by *Riigikogu* (Estonian Parliament) in December 2000.

The Human Genes Research Act ensures the highest ethical and security principles, regulating establishment and use of the database. The Act establishes the principles of voluntary participation, informed consent and a special Ethics Committee.

According to the Act the Estonian Genome Project Foundation was established on March 26, 2001 with the aim of coordinating the Estonian Genome Project - the creation of a central Gene Bank database of health and genetic data of the Estonian population. The project aims to collect the data of up to 1,000,000 people.

Systematic data collection and blood samples will lead to a unique database enabling large scale association studies, revealing new information about genes that cause and influence common diseases. This information can lead to more exact and efficient drug development, new diagnostic tests, improved individualized treatment and determination of risks of development of a disease in the future.

The key to the success of such a large scale project is in the public-private partnership between the Estonian Genome Project Foundation and EGeen. The foundation is the owner of the database and acts as a privacy shelter. EGeen, the exclusive commercial licensee of the database, will finance the project to the benefit of both parties.

Today, three years after the initial idea the first investments have been made to carry out the Pilot Project, which has been prepared up to every detail.



GOAL AND OBJECTIVES

Goal of the Project

The underlying idea of the Estonian Genome Project (EGP) is the establishment of Gene Bank - databases including phenotype and genotype data of the Estonian population - with the objective of carrying out scientific research, genetic and health studies, in order to find the genes that cause and influence common diseases.

The specific aim of the Project is to create a collection of health care status descriptions of a large part of the Estonian population, collect tissue samples of donors, create LD maps of donors, and develop software that enables the data and products of the Genome Project to be marketed.

A long-term goal of the Project is the practical implementation of systematic advances in genomics to public health at a massive scale. Provided that the data of the majority of adult population will be included into the databases emerging in the course of the Project, the impact of genomic medicine can be monitored at the whole population level.

Objectives of the Project

Since the Project has numerous facets and is closely related to many areas of life, it also has equally many outputs. From the point of view of the Estonian state, there are several objectives of the Project.

The achievement of a new level in Estonian health care, expressing itself in saving on expenditure and more efficient medical assistance; enhancement of the competitiveness of medical services in the Baltic Sea region and the preparation of health care in Estonia for new developmental directions and changes in the future.

Increase in health awareness of the population through objective genotype based risk assessment and thus, the enhancement of one's health and the helping of one's descendants and fellow citizens.

Increase in the international competitiveness of the Estonian economy - the implementation of the Project includes the development of medical, gene technology and research institutions' infrastructure, as well as investments in high technology and the creation of new jobs, and the emergence of knowledge intensive products and services in stated fields.

The supporting of the education in the field of biology, bioinformatics, social sciences and biomedicine is an important component of the Project. It will ensure the

required constant stream of qualified specialists in the high technology sector.

The supporting of the integrated development of economic and administrative areas through various possible application of gene technology, and the development of co-operation between different fields (gene technology, information technology, agriculture, health care, etc.).

The Project also includes a strong educational component - every person, despite the fact whether he/she participates in the Project or not, will receive general knowledge of genetics, either through the contribution of the media or directly from a doctor.

Competitive Advantages of the Project

In comparison with similar already existing and still intentional projects, the Estonian Genome Project has a number of advantages, the most important of these are:

- Genetically and statistically suitable population - results globally applicable;
- Basic approval and support by the government and the public;
- The relatively flexible organisation of Estonia as it is a small country;
- Well-developed primary health care sector and the possibility to access existing national healthcare databases (e.g. Cancer Register);
- High educational level of the population and their support for innovative projects;
- Developed information technology and data communication infrastructure;
- Existence of scientific and technological infrastructure and the necessary intellectual capital;
- Relatively low labour and overhead costs;
- Geographical size and logistical potential.

Relationship with the Public

Regarding the relationship with the public, the starting point for the Estonian Genome Project is to be an active party and to give as much information as possible to all target groups, which get into contact with the Project. The aim of notification activities is the general teaching of the public.

The Estonian Genome Project Foundation shall notify the public in cooperation with the Estonian Genome Foundation (www.genomics.ee), one of the aims of which is increasing the awareness of the public of developments in the field of gene technology and biotechnology in general.



LEGAL AND ETHICAL FRAMEWORK

Legal Regulations

For the success of the Project, it was agreed that it must be based on internationally acceptable norms of ethics and good practice and thus avoid fragmentation of societal solidarity and ensure public acceptability and respectability.

Legal regulations were prepared by an international working group and guidance was obtained from all available international documents dealing with genetic research, such as the UNESCO Universal Declaration on the Human Genome and Human Rights (1997) and the Council of Europe's Convention on Human Rights and Biomedicine (1997). A unique piece of legislation - Human Genes Research Act - was passed by *Riigikogu* (Estonian Parliament) on December 13, 2000.

The objective of the Act is to facilitate genetic research and regulate the establishment and maintenance of the Gene Bank and collection, processing and issuance of data. Pursuant to the Act persons shall participate in the research voluntarily and the confidentiality of the identity of gene donors shall be ensured. Further, the persons are protected from misuse of genetic data and discrimination based on the structure of their DNA and genetic risks arising therefrom.

The Act shall not apply to genetic testing performed for example for the purpose of identifying a person or diagnosing an illness. Tissue samples taken in the course of genetic testing shall not be added to the Gene Bank and it shall not be possible to use the Gene Bank for performing genetic testing at the request, for example, of a court or of an investigative body.

Main provisions of the Act:

- The Gene Bank may be used only for scientific research, research into and treatment of illnesses of gene donors, public health research and statistical purposes.
- Only a gene donor, a doctor treating the gene donor, shall have the right to receive personalised information pursuant to the requirements established by the Government of the Republic of Estonia.
- Gene donors are entitled to receive information about themselves from the Gene Bank free of charge.
- Blood samples and health and genetic data are the property of the Gene Bank. A gene donor shall not receive any remuneration for their processing.
- People shall be given an opportunity to participate in the Genome Project, but no one shall be obliged to participate. In order to make a person's self-realisation really free, he or she should be aware of his or her rights and obligations as a gene donor. Therefore, the Act stipulates the circumstances of which a gene donor should be notified before his or her blood sample is taken. Only after that, a person

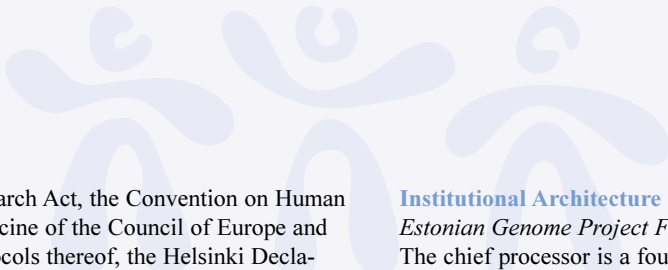
- can give a valid consent and become a gene donor.
- To ensure confidentiality of a gene donor, the personal data of the gene donor shall be separated from genetic data and each blood sample and set of health data shall be given a unique 16-digit code.
- To make the protection of the data stored in the Gene Bank more efficient, a detailed security concept has been developed.
- No one shall be discriminated against on the basis of genetic information, especially in insurance and employment relations. Such organisations shall not be issued any data.
- A gene donor shall decide whether he or she wants to know his or her genetic data or not.
- If a gene donor does not want to participate in the Genome Project anymore, he or she shall have the right to demand deletion of the data that enable identification of his or her person or, in certain cases, of all the information stored in the Gene Bank about him or her.
- After deletion of the given data, it will not be possible to associate a blood sample and a gene donor and the donor shall never receive any information about him or her.
- The law stipulates bringing up criminal charges for inducing a person to become a gene donor, carrying out illegal human research, disclosure of secret information and discrimination.
- The Gene Bank database shall not be taken outside the territory of the Republic of Estonia.
- In addition to the Human Genes Research Act, the implementation of the Genome Project is regulated by the Personal Data Protection Act and the Databases Act.

Ethical Issues

In order to treat ethical issues that might emerge during the compilation of the Gene Bank, a special Ethics Committee with advisory capacity has been formed; the members of which are experts having previously been in contact with medical ethics and medical legislation.

According to the Human Genes Research Act the Ethics Committee assesses the ethicality of the processing procedures of the Estonian Genome Project Foundation. When carrying out the Project and during the launch of later activities and research, pursuant to the Act, the decisive role will be given to the Ethics Committee, which will evaluate the pertinence of carrying out medical studies at state level.

The aim of the Ethics Committee is to assist in ensuring the protection of the health, human dignity, identity, security of person, privacy and other fundamental rights and freedoms of gene donors and resolution of general ethical problems related to human gene research. In its activities, the Ethics Committee abides by generally acknowledged ethics documents, primarily, the



Human Genes Research Act, the Convention on Human Rights and Biomedicine of the Council of Europe and the Additional Protocols thereof, the Helsinki Declaration of the World Medical Association, and the Universal Declaration on the Human Genome and Human Rights of UNESCO.

The members of the Ethics Committee are appointed and, if necessary, removed by the Supervisory Board of the Estonian Genome Project Foundation. The Supervisory Board is the highest body of the Estonian Genome Project Foundation, which consists of three Members of the *Riigikogu* (Estonian Parliament), three representatives of the Government, and three Members of the Estonian Academy of Sciences.

The task of the Ethics Committee is to draw the attention of the Supervisory and Management Boards of the Genome Project to circumstances that might be in conflict with ethical norms. Pursuant to its statutes, the Committee presents an annual report on the activities and most important opinions of the Ethics Committee to the Supervisory Board and the Management Board of the Genome Project.

Everybody can address the Ethics Committee of the Genome Project to receive information, advice or an assessment of the Committee about matters related to the Project.

Assessments and resolutions of the Ethics Committee are independent and impartial. To ensure independence, the costs of the operations of the Ethics Committee are covered with funds allocated from the state budget.

Institutional Architecture

Estonian Genome Project Foundation (Chief Processor)

The chief processor is a foundation founded pursuant to the Human Genes Research Act, by the Government of the Republic of Estonia, which has the right to organise the taking of DNA samples, to prepare descriptions of health statuses and genealogies, to code and decode, preserve, destroy and issue descriptions of health statuses and genealogies, to perform genetic research and to collect, preserve, destroy and issue genetic data.

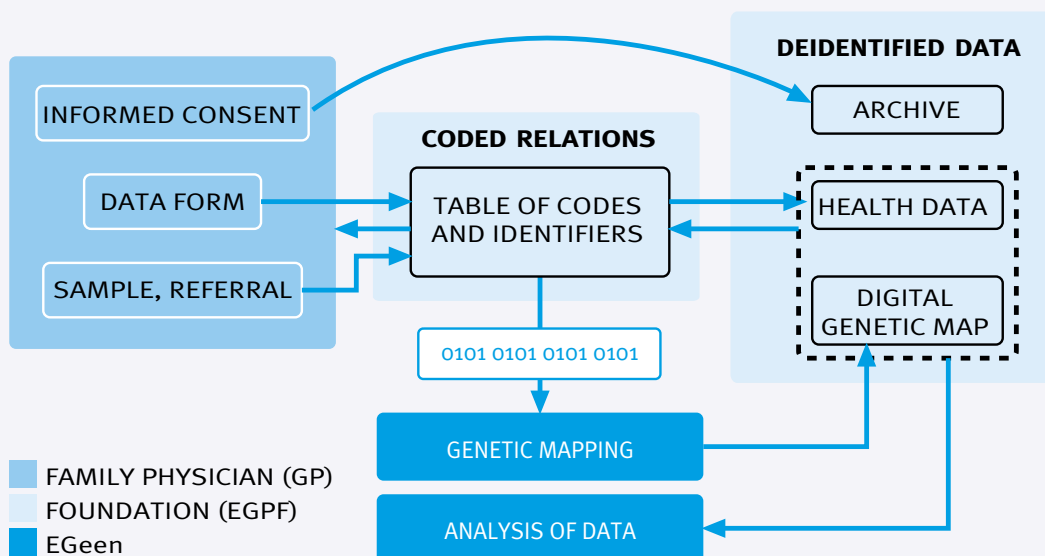
The objectives of the chief processor are to:

- promote the development of genetic research;
- collect health and genetic data of the Estonian population;
- use the results of genetic research to improve public health.

In order to achieve its objectives, the competence of the chief processor includes the establishment and maintenance of the Gene Bank. The chief processor has the right to delegate the rights of processing, except for coding and decoding, to an authorised processor on the basis of a contract in the cases and under the conditions prescribed in the Human Genes Research Act.

EGeen (Authorised Processor)

EGeen is a public limited company founded by the Estonian Genome Project Foundation to incorporate investments and mediate financing of the project. EGeen has been granted the status of an authorised processor and has received from the chief processor (EGPF), on the basis of a contract, all processing rights of the database, except the right to code and decode. Requirements for the authorised processor have been established by the Minister of Social Affairs of Estonia.





ESTABLISHMENT OF THE GENE BANK

The Estonian Gene Bank, i.e. database including phenotype and genotype data of the population, will be established during a period of five years, with the participation of up to 1 million individuals, with 70-80% of the participants being included during the first three years. The population of Estonia is 1.4 million (2000).

A special IT infrastructure and structures of databases have been created with the aim of enabling application of a digital questionnaire and collection, processing and preservation of data.

The data collection process consists of the collection of phenotype data and taking tissue samples. The collection of phenotype data, i.e. identification of phenotypes is performed by data collectors having the status of an authorised processor. Within the data collection process, matters related to the project shall be introduced to people, they shall sign the Gene Donor Consent Form, fill in the questionnaire of health status, and tissue samples shall be taken from them. The estimated time needed for filling in one questionnaire is 60 - 90 minutes. Presumably, the actual time needed for filling in the questionnaire is in most cases about a third shorter than the permitted maximum.

Informed Consent

Participation in the Gene Bank is voluntary for gene donors. Written informed consent will be obtained from the gene donor, as a result of preliminary relevant information and explanation, where he/she confirms that he/she participates in the Estonian Gene Bank on a voluntary basis and gives permission to use the clinical information collected about him/her for scientific purposes. A Gene Donor Consent Form contains information about the rights of a gene donor.

Phenotyping - Health Data Mapping

Phenotyping or health data mapping is aimed at the collection of data about the population of Estonia, concerning health status (health data) and genealogy (genealogical data), lifestyle, environmental factors and drug response.

Health and genealogical data is collected by data collectors, these are primary care physicians who have received relevant training (family physicians or general practitioners), and have the status of being the authorised processor of the Gene Bank. All data collectors have passed the data collectors training course organised by the Estonian Genome Project Foundation (EGPF).

The EGPF assists in the improvement of the hardware and software of data collectors pursuant to the needs of the project. In addition data collectors shall receive remuneration for collection of the data of Donors. The number of duly filled questionnaires and tissue samples that are submitted to the Gene Bank shall serve as the basis for remuneration.

Data collectors will perform phenotyping by interviewing subjects, and by using other medical data and records he/she might have on the individual. In parallel to the data collection, necessary for phenotyping, a blood sample is also taken from the participants in the Project. Phenotyping procedure also includes the transmission of health data into the central database, and the checking and updating of the data.

Upon collection of descriptions of health statuses, the questionnaire is filled in digitally. The general part of the questionnaire includes: socio-demographical data; genealogy; diseases; the environment and health behaviour, incl. smoking and alcohol consumption habits, physical activity, nutrition, work and home environment. Filled in questionnaires are sent electronically to the Coding Centre of the EGPF in the form of authorised and encrypted electronic documents.

International acceptability

The questionnaire has been prepared proceeding from the advisory bases for generating medical questions published by the World Health Organisation. Upon description of past diseases, it is abided by the 10th wording of the International Classification of Diseases (ICD-10).

To assess the work environment and the occupation, the international ISCO-88 classification which has been adjusted by the Estonian Statistical Office is used.

Completion of the questions of environmental factors is based on the research of the European Prospective Investigation on Cancer (EPIC).

To ensure reliability of the data, the data are monitored pursuant to the Good Clinical Practice (GCP) standards. The EGPF has developed a suitable monitoring solution for the data collection process.

The questionnaire contains filter questions at the beginning of the topics and automatic questionnaire guide pursuant to the answers given by the patient (Computer Assisted Personalized Interview - CAPI).

Integration with the family doctor software

Compatibility with the family doctor software is meant for alleviation of the workload of the data collector. The electronic data form of the questionnaire and integration into the family doctor software enables automatic verification of the existence of the data necessary for filling out the questionnaire in the electronic disease file kept by the family doctor.

Questionnaire of Health and Genealogical Data

The objective of the questionnaire of the Estonian Genome Project is to describe the data that reflect the health condition, past illnesses and their treatment, lifestyle, physical and social environment and hereditary qualities of a gene donor. The questionnaire is the same for all gene donors. Data shall be collected from about 75% of the population, both the healthy and the sick, and thus it is possible to establish suitable control groups inside the database.

Disease questionnaire

The structure of the disease part results directly from the structure of the 10th wording of the International Classification of Diseases (ICD-10). Universal and internationally understandable fixation of diseases is a basis for investigation of the genetic reasons of diseases. Filling out the disease questionnaire is started from more general areas with filter questions and if necessary, it is gradually moved deeper with more detailed questions related to the topic.

Genealogical questionnaire

The genealogical module is a separate part where data about relatives is asked in accordance with the Human Genes Research Act. On the basis of genealogical data, genealogical trees of the Estonian population are prepared when the database enables it. Close relatives include the biological parents, grandparents and the children of the parents of the gene donor. Separate questions are asked about twin brothers and sisters in order to make later processing of the data and planning for research easier.

Tissue Samples

After the questionnaires have been filled in, tissue samples shall be taken from gene donors. A tissue sample is 50 ml of venous blood that contains DNA. After blood samples are taken, they are labelled with a transportation code and transferred to the company providing transportation and logistics services.

Tissue samples are delivered to the Coding Centre of the EGPF where the temporary transportation codes are replaced with unique codes given to gene donors. Tissue samples are transferred to the Laboratory for the processing and extraction of DNA. Processing must begin within 48 hours as of the moment of taking the blood. After the quality check of DNA, blood fractionations and DNA are placed in the Storage Facility of the Gene Bank.

Coding Centre, Laboratory and Storage Facility

The Coding Centre, Laboratory and Storage Facility, are situated in a specially designed premises. The aim of the establishment of the Coding Centre is to ensure secure processing and storage of collected data. The Coding

Centre is engaged in coding the data and tissue samples received from data collectors and, in cases stipulated in the Human Genes Research Act, in decoding.

Upon arrival of Gene Donor Consent Forms to the Coding Centre, the data of gene donors is coded. Coded Consent Forms are archived at the premises of the Coding Centre.

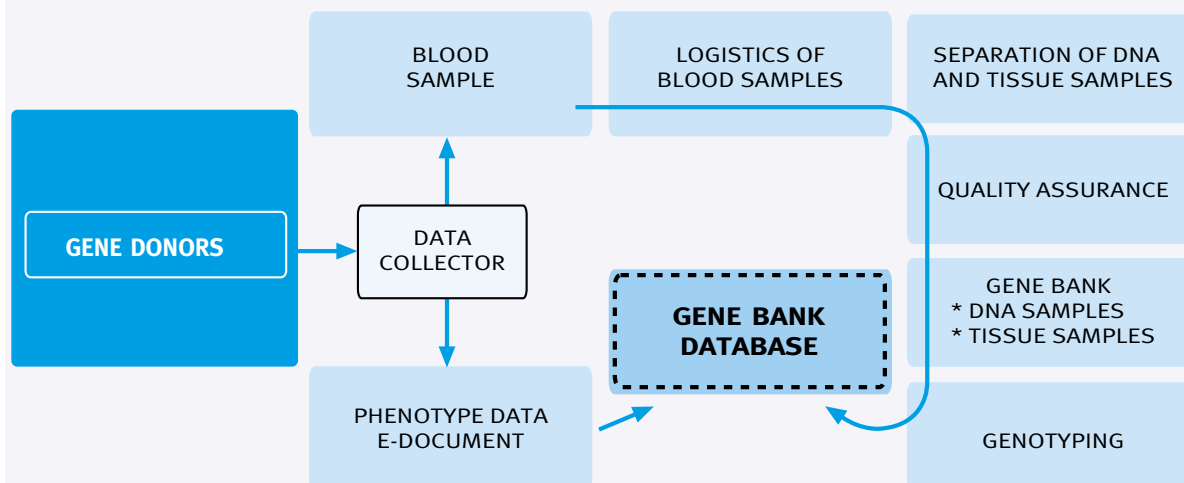
The personal data of gene donors (incl. their names, personal identification codes, birth dates and addresses) are separated from the descriptions of the health status of gene donors and they are saved in a separate database of personal data of the Coding centre. The phenotype data of questionnaires is coded with unique codes and saved in the database of the Gene Bank.

On the basis of genealogical questions of the questionnaire and using the database of personal data of the Coding Centre, the genealogical data of gene donors is identified and recorded in the database of the Gene Bank.

Genotyping - Genetic Data Mapping

Genotyping will be performed using most efficient technology available to ensure that project cost is low enough to analyze approximately 60,000 - 100,000 SNPs (single nucleotide polymorphisms) per individual. The DNA, necessary for genotyping, is isolated from blood taken by the data collectors. DNA and plasma will be kept in liquid nitrogen for further use. The average DNA yields from the 50 ml blood sample should be around 2 milligrams. This will be enough to perform the genotyping for the LD map. As a final result of genotyping, a genetic database or more precisely, LD map is created, covering 60 000 - 100 000 marker loci (SNPs) of one million people. This can be used for the large-scale association studies (e.g. case-control), on the basis of linkage disequilibrium.

The Gene Bank database, including LD map that covers 60 000 - 100 000 marker loci (SNPs) and phenotype data of one million people, enables different genetic study designs, and reduces time needed for patient recruitment to the minimum.



Monitoring and Quality System

Monitoring of the Project is carried out by trained monitors at data collection and before coding of data in the Gene Bank on the basis of the data of other databases.

The aim of monitoring is to verify that:

- 1) the rights and well-being of gene donors are protected;
- 2) the data presented in questionnaires is exact, complete and verifiable on the basis of initial data;
- 3) the Project is carried out in accordance with legal acts and other agreements;
- 4) the Project is carried out with great professional care, at a high scientific level, in accordance with acknowledged laboratory practices, and in conformity with generally acknowledged ethics requirements of scientific, genetic and medicinal product research.

Monitoring includes comparison of health and genealogical data with initial data on the basis of the random selection principle as well as monitoring the performance of contracts concluded with data collectors. The work of couriers, the laboratory and the storage facility and other work processes of the EGPF will be revised as well. The activities of monitors are ensured in accordance with international standards and they have been prepared pursuant to the ISO international quality management system.

Additionally, according to the Human Genes Research Act, the supervision of collection of descriptions of health statuses and genealogy and the supervision of processing of tissue samples, DNA descriptions, and descriptions of health statuses and genealogy is being performed by the Data Protection Inspectorate.

General Structure of the Information System

The general information system of the Gene Bank includes an information system of monitoring of the laboratory and transportation, which is to observe the movement of tissue samples from the moment they are taken up to storage of the tissue and DNA material, a supervisory system supporting the general work process of the Gene Bank, and other necessary support systems.

It shall be possible to the extent of the entire information system of the Gene Bank, to monitor the operations of each user upon insertion, change or deletion of data that is important for the Gene Bank.

Data Protection Requirements

Data in the Gene Bank shall be processed in compliance with the highest standard of data protection. Data enabling identification of gene donors shall not be available through the external computer network of the Gene Bank.

Tissue samples, descriptions of DNA or descriptions of state of health can be issued from the Gene Bank only in coded form, as a set of data and on the condition that samples or data concerning at least five gene donors are issued at a time.

Coding and Decoding

Each tissue sample, description of DNA, description of state of health and genealogy shall be given a unique code consisting of at least sixteen random characters immediately after receipt of the tissue sample, description of DNA, description of state of health or genealogy in the Gene Bank. The method of generating the codes must be approved by the data protection supervision authority.

All data concerning a tissue sample, description of DNA and description of state of health which enables the reverse identification of the gene donor, including the name, personal identification code, date of birth and residence shall be replaced with a code.

The code given to a tissue sample, description of DNA, description of state of health or genealogy shall be indicated on the written consent of the gene donor. The written consent together with the code indicated thereon in the database of the Gene Bank shall be stored and it shall be the only possible key for decoding.

It is permitted to decode data only in the following cases and for the following purposes:

- 1) in order to destroy a tissue sample, a description of DNA or a description of state of health or data which enables decoding;
- 2) in order to enable access to data on a gene donor stored in the Gene Bank, except genealogies, at the written request of the gene donor;
- 3) in order to renew, supplement or verify a description of the state of health of a gene donor without contacting the gene donor unless the gene donor has prohibited the supplementation, renewal or verification of the description of his or her state of health;
- 4) in order to identify a gene donor on the proposal of the chief processor and with the consent of the Ethics Committee, to contact the gene donor and to renew, supplement or verify a description of his or her state of health with his or her written consent;
- 5) in order to identify a gene donor and, with the gene donor's written consent, to take a new DNA sample if a tissue sample has been destroyed or does not contain sufficient DNA;
- 6) in order to identify a gene donor within the Gene Bank and amend his or her genealogy if the results of DNA research contradict the previously known genealogy or provide new information concerning the genealogy;
- 7) in order to issue a description of the state of health of a gene donor to the doctor of the gene donor at the request of the doctor of the gene donor and with the consent of the gene donor or, in urgent cases where a gene donor is unable to grant consent and has no legal representative or guardian or if the legal representative or guardian of the gene donor is unavailable, without the consent of the gene donor but in his or her interests and according to his or her presumed intentions.



RANGE OF USE AND APPLICATION

The Gene Bank may be used only for scientific research, research into and treatment of illnesses of gene donors, public health research and statistical purposes. Use of the Gene Bank for other purposes, especially to collect evidence in civil or criminal proceedings or for surveillance, is prohibited.

The Gene Bank database should be of great interest among different research institutions, bioinformatics, biotechnology and pharmaceutical companies because it enables to analyse genotype and phenotype relationship based on entire population. Researchers who are legal persons in public law or state agencies of the Republic of Estonia are granted the right to use descriptions of DNA or parts thereof without charge.

A recent research has demonstrated that the Estonian population is perfectly representative of all European (Caucasian) populations. According to the scientific paper prepared by the scientists of Wellcome Trust Center for Human Genetics, Wellcome Trust Sanger Institute, University of Michigan, Third Wave Technologies, Inc, IMCB and Estonian Biocentre, Asper Ltd and European Bioinformatics Institute (Nature 418, 544 - 548 (2002); doi:10.1038/nature00864) the genotyping data of Estonians and the others (Caucasians) and LD map of the human chromosome 22 demonstrate clearly that there are only minor differences between European populations. Meaning that if the research will be carried out based on

the genetic data of Estonians, it can be generalized for other Europeans as well.

The Gene Bank database, including LD map that covers 60 000 - 100 000 marker loci (SNPs) and phenotype data of one million people, can be used for large-scale association studies (e.g. case-control), on the basis of linkage disequilibrium. The database enables different genetic study designs, and reduces time needed for patient recruitment to the minimum. Deidentified data from the database can be compiled by using several filters.

According to the Human Genes Research Act there is a possibility to carry out further studies on the basis of the Gene Bank. Upon the approval of the objective of the further study by the Ethics Committee it is possible to identify a gene donor, in order to renew, supplement or verify a description of his or her state of health with his or her written consent. It provides the possibility for carrying out more precise association research.

The database can also be used for the benefit of the persons included in the Gene Bank, particularly in the context of family physicians, disease registers and other joint projects in order to assess health risks or determine treatment. According to the Human Genes Research Act the doctor of a gene donor has the right to obtain the decoded description of the state of health of the gene donor from the Gene Bank in order to treat the gene donor.

FINANCING OF THE PROJECT

Public-Private Partnership

The scale of the Project requires both public and private input. In order to secure funding for the project and deliver tangible pharmaceutical and health-care products, a for-profit entity EGeen was created.

In exchange for funding and granting the Estonian Genome Project Foundation a stake in the company, EGeen was granted exclusive commercial access to all data emerging from the Estonian Genome Project.

Given the scale of the project and its unique potential to catapult Estonia's healthcare system into the forefront of personalized medicine, this comprehensive and mindfully crafted public-private partnership serves a paramount role in ensuring the success of both the public project and the efforts of the private company to discover and develop products of high therapeutic value.

Pilot Project

Within the Pilot Project of the Estonian Genome Project, launched in September 2002, descriptions of health status and tissue samples of 10 000 gene donors will be collected. The Pilot Project will take place in three Estonian counties during six months and it is aiming at collecting 10 000 tissue donations. About 80 family physicians are expected to take part in the Pilot Project.

The main aim of the Pilot Project is to verify the reliability of the logistics and the data handling capabilities (incl. the work process, logistics and IT solutions of the database, the coding centre, laboratory and storage facility). After the Pilot Project has been completed, the Estonian Genome Project will be expanded all over Estonia.

Success of the Pilot Project is a precondition for carrying out the Main Project. Within the Pilot Project, only phenotype data shall be stored in the database of the Gene Bank. The Pilot Project does not include identification of genotypes and insertion of genetic data into the database of the Gene Bank. Identification of genotypes of tissue samples collected within the Pilot Project shall be performed within the Main Project.



Estonian Genome Project Foundation
Vallikraavi 2
Tartu 51003 Estonia
Tel: + 372 7 440 420
Fax: + 372 7 440 421
e-mail: geenivaramu@geenivaramu.ee
www.geenivaramu.ee

EGen International Corporation
303 Twin Dolphin Drive Ste 600
Redwood City, CA 94065
Tel: + 1 650 632 4389
Fax: + 1 650 551 9901
e-mail: egeeninc@egeeninc.com
www.egeeninc.com

Estonian Office
Vallikraavi 2
Tartu 51003 Estonia
Tel: + 372 7 440 455
Fax: + 372 7 440 455
e-mail: egeeninc@egeeninc.com
www.egeeninc.com