HUNT Biosciences

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Non-confidential Information

HUNT Biobank

May 2008

”Serious about biobanking”

Table of contents

1 BACKGROUND AND INTRODUCTION HUNT BIOBANK

1.1 The HUNT epidemiological studies

In 1984, a population-based health study was initiated in the central Norwegian region of Nord-Trøndelag. It was intended to stimulate epidemiological research and to provide a new basis for clinical and preventive medicine projects. The study was named HUNT - HelseUndersøkelsene i Nord-Trøndelag. The county of Nord-Trøndelag has a scattered rural population of about 130.000, which can be characterized as stable and homogeneous. Cities are small with <25.000 inhabitants and the population is served by two well established local hospitals. Until today, two surveys have been completed, while a third is in progress and will be finalized in 2008.

The **HUNT1** study (1984-1986) recruited 75.000 participants above 20 years of age, with no upper age limit. The participation rate reached 88% – a remarkable result hardly matched by any other study – nationally or internationally. The survey was based on questionnaires and clinical examination but no biological samples were collected.

The **HUNT2** study (1995-1997) had 74.000 participants, again achieving a very high participation rate of 72%. The age group between 13 and 20 years was included in a sub-study called *YoungHUNT*. A detailed description of the HUNT2 study design can be found in Holmen et al., 2003 (www.hunt.ntnu.no/forskning/metodeartikkel.pdf). In addition to questionnaires and clinical examination, 65.000 blood samples were collected from participants older than 20 years leading to the present collection of purified DNA material.

The ongoing third survey - **HUNT3** - was initiated in 2006 and will be completed towards the end of 2008. A participation rate of close to 60% is expected, resulting in about 60.000 participants including the Young HUNT sub-study covering the 13 to 20 year olds.

HUNT3 is expanded even further and includes additional types of biological material (see box). Comprehensive datasets covering health, disease, lifestyle and environmental factors are gathered using questionnaires and by clinical examination. HUNT3 is performed at international "best practice" level and positions the HUNT studies as a leading biobank resource. HUNT3 is supported by public grants adding up to NOK 60 Mio.

hunt 3
Helseundersøkelsen i Nord-Trøndelag

Biological material collected:

- *Serum/plasma/buffy coat (50.000)*
- *DNA on FTA-paper from the Young-HUNT population (10.000)*
- *Immortalized cells on DMSO for later cell-line production (50.000)*
- *RNA (15.000)*
- *Whole blood on Na-heparin for trace-elements/metal analysis (35.000)*
- *Fresh-frozen urine samples (15.000)*

The HUNT studies are embedded in the public Norwegian healthcare system that enables and promotes general health surveys and longitudinal studies. The system of unique personal identification numbers (PINs) allows the linkage to various National Registries providing complementary information and allowing for long-term tracking of patients.

1.2 Comprehensive medical, environmental and lifestyle information

The HUNT studies compiled extensive medical, lifestyle and environmental data associated with each biological sample and include about 800 exposure variables and nearly 3000 different variables in total per individual. These datasets allow for prospective correlations to be made between genetics, epigenetics, lifestyle, environmental factors and health / disease profiles. Through an individual personal identifier (PIN), linkage to registries at a national level (such as the National Cancer Registry, National Prescription Registry, Cause of Death Registry and the Medical Birth Registry) can be established to access additional information. Participants provided very precise information throughout the HUNT surveys. This has been validated in various studies based on HUNT data and greatly contributing to the overall value of HUNT Biobank for research projects.

The following table summarizes the data sets that have been compiled during the HUNT surveys and can be obtained from National Registries:

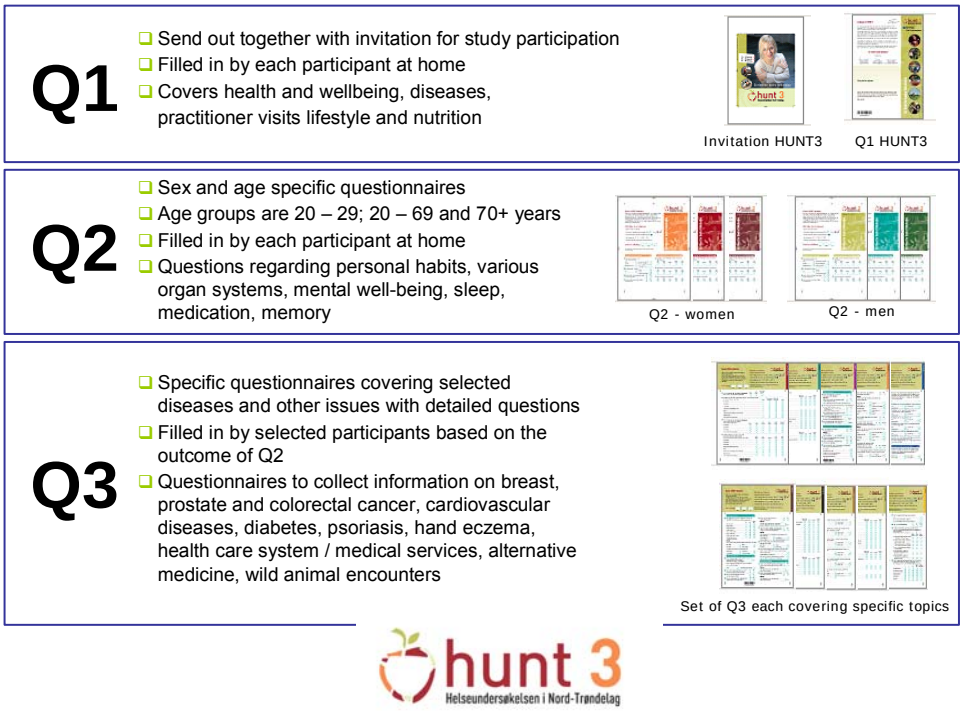
Type of information	Collected via / accessible via:	Examples of details
Measurements, Results of medical examination	Clinical examination of study participants	Height, weight, Body Mass Composition,, blood pressure, heart rate, bone density measurements, Spirometry, V02max-measurements, hearing, vision, urine analyses on microalbuminuria in samples
Laboratory values	Analysis of blood samples in clinical laboratory within 24 h time frame	Total cholesterol, HDL, triglycerides, Glucose, Creatinine, Tranferrin saturation and TSH, liver transaminases
Health and disease status	Questionnaire (Complete English versions attached)	Self reported health and disease status Progression for diabetes, lung, cardiovascular, thyroid, muscle- and skeletal diseases, mental diseases (especially anxiety and depression) Quality of life measures, migraine and other headaches, physical and mental dysfunction, prostate complaints, urine incontinence, female reproductive data i.e. on menarche, pregnancies, hormone consumption, and gynecological diseases.
Family medical histories	Questionnaire	Among siblings: Diabetes, Cardiovascular diseases, and high blood pressure Among relatives (mother, father, siblings, children): Stroke, CV disease before age of 60, Asthma, Allergy, Cancer, High blood pressure, mental problems, Osteoporosis, Diabetes and age of onset.
Living conditions, personal circumstances	Questionnaire	Type of housing, in-house environment, size of household, education, employment, economical situation, friends / social contacts, local environment and neighborhood, present well-being
Lifestyle Information	Questionnaire	Diet, smoking, alcohol consumption, drug consumption, physical activities
Clinical records and local end-point registries	Access via local hospitals	Clinical outcome from hospital records.Validation of some major cardiovasuclar diagnoses and fractures has been done for the HUNT-partcipants This is to provide information of diseases occurring after the basic screening situation to be used for prospective research purposes:
Medication	Via crosslink with National Health Registries: The Norwegian Prescription Database (est. in 01/ 2004)	The database receives electronic data on all prescriptions, reimbursed and non-reimbursed, dispensed from all the five hundred Norwegian pharmacies

Genealogy	Via crosslink with National Health Registries: *Medical Birth Registry* A national "BioHealth Norway" *genealogy database* is currently under development	The Medical Birth Registry (established in 1967) is a national health registry of all newborns in Norway set up for research and surveillance of health conditions connected to pregnancy and birth*
Cause of Death	Via crosslink with National Health Registries: *National Cause of Death Registry*	Registry established in 1922, notifications of death are scanned and coded according to international classification systems and further adapted for statistical purposes. Statistics Norway runs the Registry and has a cooperation agreement with the Norwegian Institute of Public Health
Cancer Cases	Via crosslink with National Health Registries: *Cancer Registry of Norway*	Registry has recorded cancer cases nationwide since 1953. It is a computerized comprehensive population registry matching relevant information from several sources including information about biopsies taken from each patient.

The original questionnaires used in HUNT1, 2 and 3, as well as English translations of the HUNT1 and HUNT2 questionnaires can be accessed via the internet and downloaded as PDF-files:

- http://www.hunt.ntnu.no/index.php?side=forskning/undersok/sporreskjema
- http://www.hunt.ntnu.no/index.php?side=english/healthinfo/quest

The English version of the **HUNT3** questionnaires will become available in 2008. The HUNT3 questionnaires were significantly improved and expanded based on an extensive review and design process initiated in 2003 and involving more than 100 scientific groups. Dependent on their age, sex and disease history, participants were asked to complete up to three questionnaires – the approach developed for HUNT3 is illustrated in the scheme below:



1.3 Longitudinal data contribute significantly to the value of HUNT Biobank

HUNT Biobank offers unique opportunities for longitudinal studies: 46.000 individuals participated in both HUNT1 and 2 covering a 10 year time frame. Out of these an estimated number of 20.000 individuals will also participate in HUNT3, resulting in the coverage of more than 20 years of their lives. It is estimated, that 30.000 HUNT2 participants will also participate in HUNT3 resulting in datasets and biological samples framing another 10 year interval. Many participants reached defined clinical endpoints during these observation periods:

- Myocardial Infarction (1996 – 2006): 300-350 annual incident cases
- Stroke: Retrospectively 1990-1996, Prospectively registered from 2004
- Venous Thromboembolism: 750 cases between 1996-2000, further registration is ongoing
- Cancer: The HUNT studies are part of CONOR (the "Cohort of Norway") covering a total of more than 170.000 individuals that participated in population based health surveys between 1994 and 2003. The follow up of CONOR cohort members revealed that a total of 15.077 cancers have been diagnosed between 1994 and March 2006 with 2.200 cases of colorectal cancer, 1.600 cases of prostate cancer and 1.200 breast cancer cases. DNA is available from 173.000 participants. By 2008, the CONOR cohort will have increased to 230.000 individuals due to the recent HUNT3 and Tromsø6 studies

For additional clinical endpoints such as diabetes, cardiovascular, gastrointestinal, and rheumatologic diseases and Multiple Sclerosis, validated data sets can be obtained. The various medical, environmental and lifestyle data monitored by HUNT since 1984 allow for prospective correlations to be made between genetics, epigenetics and health / disease profiles positioning HUNT as a leading resource for prospective population based studies.

2 CONSENT AND PROJECT APPROVAL

2.1 Informed Consent

Participation in the HUNT Studies is voluntary and based on informed consent. The participants were informed through a personal letter and an information folder, followed by personal information at the screening sites and general information via media, i.e. newspapers, radio, television as well as the comprehensive HUNT homepage. The homepage is also used as general information platform with regular updates about ongoing research activities. Each participant signs a **written informed consent** regarding the screening, subsequent controls and follow-up, and the use of data and blood samples for research purposes. Participants also consent to linking their data to other registries (subject to approval of the Data Inspectorate). The data files and samples are **de-identified** using coding systems.

The original **consent form** signed by **HUNT2** participants between 1995 and 1996 was dictated by the Data Inspectorate and did not specify the use of samples in genetic research. It required a new consent if the blood samples were used for medical research. A **revised consent form** (1996-1997) was used after the Data Inspectorate realized the difficulties with this limitation. The new wording states that blood samples can be used for research without a new consent if the regional ethics committee approves the research. However, the option for genetic research was still not included (*Appendix 1*).

In 2002, an information leaflet was sent out to all HUNT2 participants (regardless of which consent had been signed), to inform them that their DNA may be used in genetic research. Participants objecting to this were invited to notify the HUNT study and withdraw their samples from the Biobank *(Appendix 2)*. This approach of non-active consent was approved by the Data Inspectorate because of difficulties with active re-consenting unrelated to objections towards genetic research and the complexities associated with the two original consent forms. The current protocol is to apply to the Data Inspectorate on a case-by case basis for using HUNT2 samples in genetic research.

For the **HUNT3 study** a new and updated information folder has been prepared. The information folder provides the basis for a broad based **informed consent** that covers research - including genetic research - in various areas and diseases *(Appendix 3)*.

2.2 Withdrawal of consent

Participants can **withdraw** their consent any time and without giving any reason. The present practice at HUNT Research Centre is that withdrawal of consent will lead to the deletion of data and the destruction of the biological material. However, a withdrawal of consent will not have retroactive effect, i.e. **ongoing projects keep the de-identified data and material**. This practice provides a reliable framework for collaboration partners and guarantees the realization of projects without restrictions.

2.3 Approval of the HUNT Studies

The Data Inspectorate of Norway and the Central Norway Regional Committee for Medical and Health Research Ethics in Norway (REK) have approved the HUNT2 samples for genetic studies. The information generated in the HUNT studies is treated according to the guidelines of the Data Inspectorate.

A similar approval has been obtained for the HUNT3 study by the Data Inspectorate and the Regional Committee for Medical and Health Research Ethics.

2.4 Existing consent covers projects with commercial partners

Importantly, the Central Norwegian REK recently decided that biological material and data generated in the HUNT surveys can be used in projects with commercial partners based on the existing informed consent *(Appendix 4)*.

2.5 Project approval

Projects using biological material and data from the HUNT studies have to be approved by the **Regional Committee for Medical and Health Research Ethics (REK).** The members of the committee are experts for their specific area of responsibility, experts with a background in ethics and law as well as a number of lay members. They are appointed by the Ministry of Education, Research and Church Affairs.

Currently the **Data Inspectorate** has to give a separate approval if genetic analysis is part of study. The Data Inspectorate is an independent administrative body under the Norwegian Ministry of Labor and Government Administration to ensure enforcement of the Personal Data Act of 2000. The purpose of this Act is to protect persons from violation of their right to privacy through the processing of personal data.

If data from other (national) health registries shall be accessed and merged with HUNT data, the approval from **The Directorate for Health and Social Affairs** is required.

2.6 New law simplifying project approval from 2008 onwards

Biobanking in Norway is regulated by the Norwegian Act on Biobanks (July 2003) ensuring that the collection, storage, processing and destruction of biobank materials are performed in an ethically justifiable manner, and that biobanks are used for the best of the individual and society. Currently a new law regulating health-related research (Helseforskningslov) is in preparation and will be implemented in 2008. The new law will simplify administrative processes by naming a single approval body (the responsible REK) for coordination of the entire process. The new law paves the way for a more streamlined and simplified process to support research projects based on Biobank data and material.

NOTE: *English translations of relevant documents are provided as appendices – the original documents in Norwegian are available on demand.*

3 SAMPLE COLLECTION, PROCESSING AND STORAGE

3.1 The National Biobank: Infrastructure and instrumentation

All biospecimens from the HUNT surveys are collected, processed and stored at the National Norwegian Biobank in Levanger that was officially opened in March 2007. It is a new building of close to 2000 m² specially designed for this purpose and equipped with state-of-the art infrastructure. The National Biobank serves as central repository for the Norwegian Health surveys collectively forming CONOR, the Cohort of Norway, comprising samples and data form about 170.000 individuals. The Biobank is operated by a staff of 15 employees with Professor Kristian Hveem (MD PhD) being the CEO.

A completely **automated sample storage and retrieval facility** for DNA samples operating at -20°C is currently installed by REMP AG (Switzerland) and will become operational within the first half of 2008.

The Biobank is using the **Nautilus LIMS** (Laboratory Information Management System) developed by Thermo Electron Corporation for the management and logistics of HUNT3 samples. This includes the login of samples using data files from the screening stations, the full hierarchical tracing of HUNT3 participants (de-identified) and the related samples and aliquots as well as auditing tables logging changes of data associated with the HUNT3 material. The use of the LIMS will be expanded to embrace data of all samples stored in the Biobank and to integrate the automated sample storage system that is currently installed. The LIMS is integrated with a **fully automated sample fractionation and aliquotting system** operating at 4°C. The unit has been developed and implemented by RTS® (Robotic Technology Systems, UK) and is currently used for processing the HUNT3 samples.

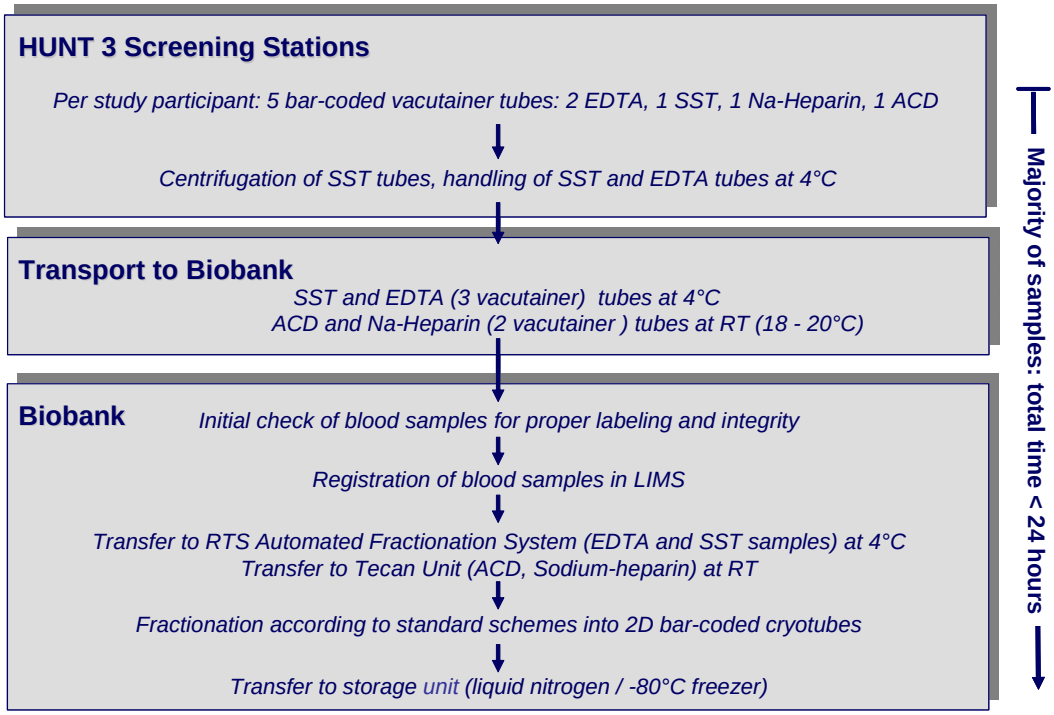
3.2 Sample collection and processing routines

3.2.1 Sample collection HUNT2 survey

In **HUNT2** blood samples were taken at a non-fasting or "random" state. Between August 1995 and June 1996 one whole blood sample (7, 5 ml) was drawn from each participant, serum was separated by centrifugation at the screening site. The samples were sent to Levanger Hospital and arrived at the Central Laboratory usually the same day or the next day serum samples were subjected to some basic biochemical analysis. Subsequently, the remaining part of the serum was stored in cryotubes at –80°C. Clots were also stored at –80°C with strict cold chain monitoring being in place. Between August 1996 and June 1997 an additional vacutainer tube of EDTA whole blood was drawn from each participant and stored in the biobank at –80°C instead of the clot. While all HUNT studies have been performed with great care and high quality, HUNT1 and HUNT2 were not designed to meet the current quality assurance and standardization measures provided for the HUNT 3 study. However, recent publicatons (*see Ref. 1 - 2 for recent Nature Genetics and Nature publications*) have shown that isolated DNA from the HUNT2 study is of very good quality and well suited for all gentic analysis including GWAS.

3.2.2 Sample collection HUNT3 survey

The ongoing HUNT3 study follows strictly standardized protocols and is performed according to state-of-the art procedures for sample collection, transport, processing and storage. Many processes have been aligned with UK Biobank protocols – one example is the fully automated fractionation system developed with RTS that ensures standardized and rapid sample processing at the Biobank. The following chart summarizes the sample collection and processing routines implemented for HUNT3:



3.2.3 Urine and tumor samples in HUNT3

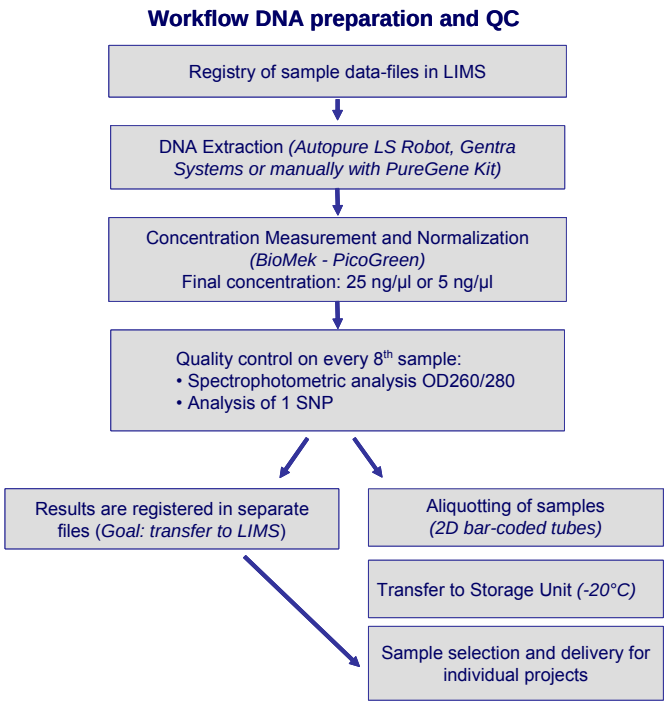
In addition to blood, **urine samples** are collected from about 10-15.000 HUNT3 participants and frozen immediately. St.Olav Hospital (University Hospital Trondheim) developed the protocol for the collection and freezing of urine samples at the screening stations. A protocol for handling the samples after their arrival at the biobank is under development as part of HUNT´s EQS-system.

HUNT collaborates with the two local hospitals to start collecting **fresh frozen tumor samples** for designated cancers (*e.g.* prostate, colon and breast cancer). Of particular interest are samples from these patients that have participated in the HUNT studies prior to the development of their cancers. Paraffin-embedded samples are already available.

3.3 DNA Preparation and quality control

DNA was isolated between 2002 and 2006 from **65.000** samples collected in HUNT2. Standard protocols for DNA extraction and quality control were developed and implemented for processing these samples.

The Biobank has manual (based on Gentra Puregene blood kit, QIAGEN) as well as **automated DNA isolation** facilities (*Autopure LS robot – QIAGEN, former Gentra systems)* with a throughput of 200-300 samples per day. The Biobank uses a robotic system (Biomek NX from Beckman Coulter) for assessment of **DNA quality** and yield also having a throughput of 200-300 per day. DNA concentration for each sample is determined by pico green / standard curve measurements. Based on these results DNA concentrations are normalized to either 5ng/µl or 25ng/µl. Every sample is measured spectrophotometrically (Nanodrop, ND-1000) to determine the OD260/280 ratio for quality assessment and for an independent concentration determination.



SNP analyses for quality control are performed on every 8th sample with either Roche's Light Cycler System offering a capacity of 160 samples per day or with the recently installed 7900HT FAST real time PCR System. This system is based on TaqMan-probe technology with end-point readings and at the present set-up the throughput is approximately 3000 SNPs a day. HUNT Biobank successfully participated in several large-scale international collaborations (e.g. FUSION Study for Type II Diabetes, Cancer-focused projects sponsored by IARC and NCI) thereby receiving external validation for the quality of the HUNT samples.

3.4 Sample selection and delivery

The Biobank has established standard protocols for the selection, quality control and delivery of samples for internal and external projects. These will be further improved after the final implementation of the automated sample storage and retrieval system in 2008.

3.5 Quality assurance and ISO certification

3.5.1 Extend Quality System (EQS) for professional SOP and document management

HUNT Biobank uses a web-based document control system called EQS (Extend Quality System) for the management of all documents and process descriptions relevant for the Biobank including its SOPs.

The EQS ensures that:

- Each user has the latest version of a document
- Users get a message when new documents are being made, or when existing documents are updated

- Each user has access to all documents relevant for his area of responsibility
- Preparation, hearings, and approval of documents occurs efficiently and with as little manual work as possible for the users
- All historical versions of a document are stored and stay available for the person in charge of the system

3.5.2 Generation and approval of SOPs

The SOPs are developed and updated in collaboration between the responsible lab technician, the responsible lab leader, HUNT Biobank´s CSO (Professor in Molecular Biology) and CEO (Professor in Clinical Epidemiology). So far alle the SOPs are accessible through the EQS-system, but will also be available through HUNT´s web site in the near future. The SOPs related to scientific tasks, are approved by the responsible scientist or the one he/she authorizes before they are entered into the EQS.

All EQS-procedures and the SOPs related to technical management and administrative tasks are approved by the administrative leader or the one he/she authorizes. Procedures are approved after the document has been circulated for comments to the relevant users or the one responsible for the relevant area in the biobank.

3.5.3 ISO certification: Status and outlook

The Biobank is working towards the ISO17025 accreditation, but initially the goal is to be certified by the ISO 9001:2000 Standard. The ISO17025 accreditation that eventually will be in place will include the sample repository as well as the data bank under same management regime. For the repository, the initial accreditation will comprise DNA isolation, storage and retrieval. Currently SOPs are being adopted according to ISO17025 requirements. The SOPs are prepared in Norwegian, but English translations will be generated to allow for review by industry customers.

4 SELECTED PUBLICATIONS

HUNT material has been used as the basis of more than 250 epidemiological studies across a wide range of clinical indications to date, and around 170 collaborative projects are currently in progress.

Historically, special emphasis has been put on the following diseases: Diabetes type 2[1,3-5,8-10], cardiovascular and kidney diseases [6,7,11-18], body weight[10;19], lung diseases and bone density[20-26]. Comprehensive data have also been generated on urine incontinence [27;28], hemochromatosis[29-32], dyspepsia[33-38], thyroid diseases[39], headache and musculoskeletal complaints[39-55] as well as for anxiety and depression [56-63].

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Overall around 500 publications were based on the HUNT studies and so far 40 Ph.D. have been completed using data and material from the HUNT studies.

5 APPENDIX

App 1: Informed consent signed by participants of HUNT2 survey (1995-97)

Translated from SAMTYKKEERKLÆRING HUNT2 (1995 – 1996 and 1996 -1997)

I understand the purpose of this health study as described in the *"Health Study in Nord-Trøndelag – an opportunity for you"* brochure. I have received the brochure "hunt – special", which deals with the various examinations I may be offered. I understand that information about me will be handled with the utmost confidentiality and that the study has been approved by The Data Inspectorate and has been submitted to the Regional Committee for Medical Research Ethics. There is no clear timeframe as to how long the information can be stored, but I understand that I, at any time, can withdraw from the study and, in addition, the information concerning me will not be used if I so choose.

1. I hereby give my consent for the results from my blood tests and other sections of the study to be sent to the doctor whose name I have given on the questionnaire.

2. If I have not given the name of a doctor, or my doctor is not participating in this study, I give my consent for the information pertaining to me to be sent to the chief municipal medical officer.

3. I hereby give my consent that I be offered the opportunity to participate in extra examinations and to be contacted by a doctor in regards to treatment or to prevent illness.

4. I hereby give my consent for the results from my participation in this study to be used in medical research and that this may include comparing this information with information from other health and disease registries or with my data from previous health studies in Nord-Trøndelag. My name and national identity number will not be identifiable with my information when the data is compared.

5. I hereby give my consent for the storage of blood samples. My consent will be procured if the blood sample I have provided will be used for medical research.

Please draw a line through any paragraphs that contain information that you are not consenting to.

Revised version of paragraph 5 used after June 1996 after consultation with Data Inspectorate:

5. I hereby give my consent for the storage of my blood samples. The approval of The Data Inspectorate and the Regional Committee for Medical Research Ethics is necessary before using my blood samples.

App 2: Information Leaflet and renewed consent for HUNT2, April 2002

Translated from "Til deg som deltok ved HUNT 2 (1995-1997)"

To you who participated in HUNT 2 (1995-1997), Verdal, April 2002

Some years ago (1995-97) you participated in the Health Study in Nord-Trøndelag (HUNT) along with over 70,000 people from Nord-Trøndelag. HUNT today is an extremely valuable source of information about health and disease. Your participation in HUNT is very important for this work.

At the health study, blood samples were taken from participants who came to the examination and were 20 years old or older. Some of the blood samples were used to examine your health, and those results were sent to you. The remainders of blood samples were stored to be used in research. These various stages were completed in accordance with the informed consent you signed at the examination.

Blood samples can inform about causes for disease

Blood samples are important in the work of finding the causes of disease. Recently, one field of research has become particularly relevant: Studies on the interaction of environment and genetics, especially in regards to preventing disease. Technological development in this area has moved more quickly than we could foresee. These technological developments present opportunities to examine the relationship between genetic factors and disease. We would like to inform you of this and have therefore included a brochure with more information.

Personal information protection and approval from the ethical committee

We wish to emphasize that all information that is collected in HUNT is confidential and is handled according to the applicable regulations and laws. Before being used in research, all blood samples are made anonymous. This means that results from the research cannot be traced back to an individual. All projects that use HUNT data, regardless of what type of data they use, must be approved by The Data Inspectorate and the Regional Committee for Medical Research Ethics. The type of analyses to be performed, how the results of the analyses will be stored, and how they will be presented to the relevant research groups are taken into consideration for approval.

Renewed Informed Consent

On the back of this letter you will find the inform consent form that you signed when you participated in HUNT. We ask you to renew your informed consent because two versions of the informed consent forms were used; item 5 was formulated differently on them. We ask therefore that you give consent that your stored blood sample still be able to be used in medical research, including analysis of genes and the study of genetic-environmental interaction. Blood samples will not be used in research that involves cloning, gene modification or other gene technology that is being publicly debated.

If you give your consent for your blood sample to be used in medical research, do not send in the response slip. We remind you that if in the future you don't want your sample or data to be used in research, you need not give a reason and you can withdraw your consent at any time.

If you do not give your consent for your blood sample to be used in medical research, you must inform us. We ask that you sign the response slip below, cut it off this letter on the line, and send it to us in the accompanying, stamped envelope by 01.05.02.

The text of the informed consent as (see Appendix 2) is quoted in the leaflet and accompanied by the following paragraphs:

The two first items of the informed consent form are no longer relevant. We therefore ask that you give consent that your blood sample be stored and used in medical research in accordance with the informed consent (items 3, 4, and 5) inside the box. If you give your consent, you need not respond to this letter.

If you choose not to allow your blood sample to be stored as stated in items 3, 4, and 5 in the informed consent, you must inform us by sending in the response slip on this letter within the time-limit (see the opposite side of this page).

Sincerely,

Geir Stene-Larsen
Norwegian Institute of Public Health

Jostein Holmen
HUNT Research Centre, NTNU

▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪ Response slip ▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪ cut here ▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪▪

I do not want my blood sample stored and used for medical research.
My blood sample should be removed and destroyed.

_____ _____
Place and date Name

App 3: Information Leaflet - informed consent HUNT3

Consent
Participation in HUNT 3 and in other public health surveys is voluntary. Every participant is required to sign an informed consent form before information from the survey can be used for research. You are asked to sign a consent form when you first come to the examination site. Information and samples collected will be stored for an unspecified time. They may be used in future projects that are at this time not yet planned provided that the project conforms to the applicable laws and regulations. In the future you will receive information about new research projects that use data from HUNT. This information will be posted on the internet at www.hunt.ntnu.no. In addition, this information will be sent out in written form to all inhabitants of Nord-Trøndelag once a year. The media will also present information about research projects connected to HUNT material. You can at any time after the survey recant your consent and request that your data is erased from the files and your samples destroyed. If you want to withdraw your consent, contact HUNT Research Centre, Neptunveien 1, 7650 Verdal, telephone number: 74 07 51 80, fax: 74 07 51 81 or e-mail: hunt@medisin.ntnu.no.
If you request that your data or samples not be used in certain types of research, it will not be used.

Consent Renewal
If in the future the data is used in research of new topics that are not described in this brochure, it may be necessary to request that your consent be renewed. If this occurs, we will send you a letter. You may be asked to provide us with a renewed consent if research projects involving private parties in genetic research are planned. This type of collaborative research is subject to public regulations and laws. Under no conditions are blood samples or any other type of biological material to be sold.

Personal Information Protection and Security
All information will be treated with respect for the protection of personal privacy and participants' private lives and in accordance with the regulations and laws. The collected information, blood samples, and urine specimens are labeled and stored without using the participant's identity (anonymous). Researchers who later use the data do not have access to participants' names, birthdates or national identity number. All those working with this public health survey are obligated to maintain professional confidentiality. The Data Inspectorate ensures that the laws and regulations concerning storage and use of health survey information are followed. HUNT3 is regulated by The Data Inspectorate.

Ethical approval
All research projects must be approved by an ethics committee. The committee is an independent body that ensures that the ethical aspect of research projects is evaluated. HUNT3 is approved by the Regional Committee for Medical Research Ethics, Central Norway. All future research projects that use data from HUNT must also be approved.

HUNT databank
HUNT database consists of information that has been collected during HUNT1, 2, and 3 by means of questionnaires, examinations, and analysis of blood and urine specimens. If you participated in HUNT1 or HUNT2, your data will be placed with your data from HUNT3. Genetic material is stored at HUNT Biobank. The purpose of the Biobank is that, in the future, samples can be withdrawn for various analyses and be compared to the results of other data in the HUNT database. As a result there will be new data entered into the database. When researchers receive data from the HUNT database, names, personal identification numbers, and other distinguishing characteristics will not accompany the data. This way the participant who gave the information cannot be identified.

Data comparison with other records and registries
For certain research projects it may be necessary to use the data from HUNT in conjunction with other public registries, for example The Prescription Registry of Norway, The Norwegian Institute of Public Health, The Cancer Registry of Norway and Cause of Death Registry. HUNT data may also be cross-referenced or compared to other types of records from Statistics Norway, for example records concerning the environment, population, education, income, public welfare benefits, labor force participation and other conditions that may affect health. In addition, some research may include obtaining diagnosis data such as upper femur fracture, cardiac infarction, stroke or pulmonary disease at primary health care services, the hospitals in Nord-Trøndelag, and St. Olav's Hospital. Some research projects may include comparing information from parents with that of their children, siblings, parents, and grandparents if they also participated in HUNT. All these various data comparisons require consent and/or preapproval by public authorities as required by the law, such as the Regional Committee for Medical Research Ethics, The Data Inspectorate, The Directorate for Health and Social Welfare or The Norwegian Labor and Welfare Organization. All information will be treated with respect for the protection of personal privacy and participants' private lives and in accordance with the regulations and laws. No researchers will know which participants provided the information.

Compensation
There is very little risk that a participant will be injured as a result of the survey. However, if this occurs, compensation can be applied for through The Norwegian System of Compensation to Patients (NPE). NPE processes compensation claims for patients who have been injured in the public health care system.

Young-HUNT
All young people between the ages of 13 to19 in Nord-Trøndelag are invited to participate in Young-HUNT. The survey, filling out the questionnaires and clinical examinations, is carried out at the schools during regular school hours. Adolescents and their parents will receive information about Young-HUNT from the school.

App 4: REK approval for using HUNT material and data in commercial projects

These paragraphs are translated from a larger work entitled Helseundersøkelsen i Nord-Trøndelag, oppdragsforskning / kommersialisering.

The committee is of the opinion that commercial activities/business activities may be carried out given that they are implemented under full public control and in a way that benefits patients.
The committee has concluded that it is not necessary to collect new, formal informed consent. Organizing the commercialization as suggested by the committee will ensure optimal use of the collected material and data. Proper medical research is expensive, and it is unlikely that government funding can supply the necessary funds for maximum utilization of the material and data in the HUNT Research Biobank. The committee does not distinguish between financial support for a project from a pharmaceutical company or a public institution such as a university. The difference may be in the scope and depth, not in how the project is outline and controlled. Moreover, the research done by pharmaceutical companies uses large quantities of biological materials in their studies, which must be approved by the Regional Committee for Medical Research Ethics (REK).
There will not be fundamental differences in the securing of rights and patents. Universities and their employees and the pharmaceutical industry will be able to apply for patents at the same level and using the same criteria based in results and data generated from the research projects. If there is income from use of HUNT and its collected material and data, the entire sum will go to HUNT, which is publicly owned.
The committee suggests that a letter be sent to all participants of HUNT that informs them of HUNT Bioscience, its purpose, its organization model, and use of possible profits. This should not be a descriptive letter presented as a request for passive informed consent. Were the participants to think that a new informed consent was necessary, it would create uncertainty and doubt. It is best to present it as it is - a possibility to accomplish research with greater scope and depth.