EpiHealth Ethics Policy

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EpiHealth - Purpose and overview

EpiHealth (Epidemiology for Health) cohort study is a collaboration between the Uppsala and Lund Universities aiming at building a large, nationwide resource for the study of the interplay between environmental factors and genes regarding the major common disorders seen in the elderly. This research resource could however be used for other research questions not included in the major aim.

The aim is to collect data from 300,000 randomly selected inhabitants in Sweden in the ages 45 to 75 years. The collection of data will start in Uppsala and Malmö, but the intention is to in the future recruit subjects also from other parts of the country. The intention is to start the inclusion of patients during spring 2011. The collection of data includes a web-based questionnaire regarding environmental factors, a visit to a test centre for collection of blood and DNA samples to a biobank and measurements of several physiological and biochemistry variables. The last step is a feedback on these latter variables to the investigated subjects.

A similar project has already been initiated in Sweden, the LifeGene study (www.lifegene.se). LifeGene has the intention to investigate half a million Swedes in the age range of 0 to 45 years. The major aim of the two studies is very similar although LifeGene from start focus on disorders affecting younger subjects. The two studies have a common infrastructure in terms of computerized handling of the questionnaire and other collected data, as well as biobanking.

Since EpiHealth and LifeGene share so many features and major aim and in terms of the populations studied are complementary, it is essential that the two studies share a common ethic policy in order to ensure that these two databases could be used in concert in the future in the study of the entire lifespan of the Swedish population. Therefore, the following document is based on the Ethics Policy document from LifeGene published in September 2011, which could be found in its original form at the home-page of LifeGene. However, due to the differences of recruitment, investigations and age of the populations between the studies, the present document also includes its unique parts.

As with LifeGene, the EpiHealth study ethical policy is based on the **Helsinki declaration** from 1964 on studies on human volunteers (revised October 2008), as well as the Swedish legalization governing the handling of personal data (**the Personal Data Act**), gene information (**Genetic Integrity Act**) and biobanking (**the Biobank Act**). The EpiHealth study will work in close collaboration with the relevant Ethics Committees.

I. Relationship with participants

A. RECRUITMENT

1. General principles

EpiHealth aims to recruit 300,000 people aged 45-75 years from all over Sweden. This must be done in a manner that respects the integrity of the participants. For EpiHealth, the rights and wellbeing of the participants prevail over the research interest of EpiHealth and its users. In order to ensure this, EpiHealth will adopt strict and well-established norms of transparency, accountability and consent in relation to its participants.

Participation in EpiHealth is voluntary. All aspects of recruitment, from initial contact with potential participants to enrolment at the baseline test center visit, will be conducted in a way that preserves the voluntary nature of participation.

In order to generate scientifically valid results, EpiHealth must also obtain agreement from participants for examination of the progress of their health, disease and incapacitation in depth and over time. This means that EpiHealth will regularly initiate re-contact with the participants and gain access to medical records. This will be made clear to the participants from the outset. They will be given the opportunity to opt out of biobanking of blood samples, biobanking of DNA, merging with official registers and national quality control registries in order to gain the information specified in the EpiHealth information brochure, merging with medical records, and EpiHealth re-contacting them for future data collections, at large should they choose. Participation in EpiHealth can be completely withdrawn and EpiHealth will then not contact the participant again, already collected data and samples will not be used in future analyses, and EpiHealth will not collect any further information about the participant. Again, this follows the line of voluntary participation in EpiHealth.

2. Selection and approach

EpiHealth will seek to recruit a random sample of the Swedish general population. Although the focus of EpiHealth is common diseases, no recruitment selection will be performed so as to target any specific diseases.

EpiHealth will identify potential participants from official registries. These contact details will be processed in confidence by EpiHealth in accordance with the Personal Data Act. Potential participants will then be sent information about the study and invited to participate.

3. Enrolment

Potential participants will receive, by postal mail, information about EpiHealth and an invitation to participate in the study. Further information will be available from EpiHealth through a free telephone service and a website (www.epihealth.se), no yet in use).

The invitation letter will include instructions on how to enroll on the web. During the test center visit the complete consent will be signed. Here EpiHealth staff will answer questions, provide clarifications and explain the consent process. If an individual then decides to take part, their signed consent will be sought and recorded before they are enrolled.

Enrolment will involve completing a questionnaire about lifestyle (e.g. diet, exercise, smoking, alcohol, job situation etc.) and other factors (such as cognitive function and medical history, etc.), executing physical measurements (e.g. blood pressure, weight, lung function, etc.) and giving blood samples.

B. UNDERSTANDINGS AND CONSENT

1. Consent

Consent will be sought to participate in EpiHealth. Participation will be presented as an opportunity to contribute to a resource that may, in the long term, help enhance other people's health. Because it will be impossible to anticipate all future research uses, consent will be sought for research in general that is consistent with EpiHealth ´s stated purpose.

Consent will be based on an explanation and understanding of, amongst other things:

- The purpose of EpiHealth, the fact that it is a long-term research resource (not a health care program), and any risks and benefits of taking part.
- The kinds of information and samples that will be collected, which may include data that some participants consider especially sensitive (with options to avoid certain questions and measurements).
- The expectation that genetic analysis will subsequently be performed on samples by researchers.
- The fact that there will be an optional link to relevant health records (past and ongoing) and the need for participants to allow such linkage for as long as possible to maximize the value of EpiHealth as a research resource.
- The kind of safeguards that will be maintained, including secure storage of data and samples (as explained in Section 8), and restricted access to data and samples.

- The assurance that only researchers that have been approved by both EpiHealth and a relevant Ethics Committee will be allowed access to the data and samples, and that data and samples will be coded before being provided to researchers, (unless a court order demands that samples be released to authorities [e.g. police]), that researchers outside EU/EES can, in collaboration with Swedish researchers, apply to use EpiHealth.

- The expectation of being re-contacted in the future by EpiHealth (optional) and the purpose of such contacts as well as the expectation that other studies connected to EpiHealth may initiate contact for other/additional studies.

- The intention to continue to hold and allow researchers access to data and samples after participants lose mental capacity or die, as such data and samples are crucial for research on severe illnesses.

- The right to partially or completely withdraw consent at any time without having to give a reason and without penalty, and the meaning of different levels of withdrawal of consent.

- The circumstances in which healthcare information about individual participants may be feedback and the options to get such feedback.

- EpiHealth´s commitment to maintaining active engagement with participants and society in general.

- Information about how to contact EpiHealth in case of questions and where more information can be found.

EpiHealth will do its outmost to make sure that participants understand what they are consenting to when they agree to take part. This will be done by ensuring recruited personnel are trained in communicating the information and assessing the understanding of participants.

The consent to participate in EpiHealth will apply throughout the lifetime of EpiHealth unless the participant chooses to withdraw. New consent will be sought for any proposed activities that do not fall within the existing consent.

2. Collection of data from relevant records

The ability to accumulate data from relevant health-records will be essential for the success of EpiHealth. EpiHealth wants to track health events, the development of disease, and the course of treatments. Thus, EpiHealth must aim to obtain such information as diagnostic codes and prescribing data. The range of different records that can be accessed will be determined by developments in the health service electronic records systems.

EpiHealth will collect data from public health care record systems (e.g. primary care, hospital, dental, prescription records and national registries, such as Cause of Death Register, Population register, Multigeneration Register, Hospital Discharge Register,

Outpatient visits register, Prescription Register, Cancer Register, Medical Birth and Malformations Register, Infectious Disease register) and national quality registries. Access to such records, at least in some instances, as well as the establishment of EpiHealth´s biobank in general, will require the approval of The National Board of Health and Welfare. During the consent process EpiHealth can (if the participant so wishes) explain what kinds of record systems it will seek access to. Psychiatric records can be considered to be especially sensitive, due to the nature of the information that such records contain. The extent to which EpiHealth will collect psychiatric records has to be clearly defined, balancing the privacy of the individual and the interest of research.

EpiHealth will not be able to say in advance which data from these various records will be needed. Although, in general, only parts of these health-relevant records will be used, the consent will cover access to the full records. This will include past records, since these will help to characterize participants and to understand later health events more completely. The full records may also be required when it is necessary to verify the accuracy of data.

3. Provision of health information to participants

EpiHealth will aim to ensure that participants understand that enrolment does not provide them with a general health check. EpiHealth is primarily a research endeavor and not a health care screening program in the clinical setting. For instance, at the test center, personnel are not primarily physicians and do not have access to full medical records. Biochemical tests and physiological variables will therefore only provide written information regarding biochemical tests and physiological variables following completion of the data collection. This does not mean that the participants will not gain from the feedback given, but it should be emphasized that only some specific tests are performed, selected from the research purpose of the study.

A printed report will be provided within three weeks following their visit to the test centre and completion of the questionnaire as a mean of feedback. The report will be available through the personal web page of the participants, or if preferred by the participant, sent by postal mail. By reporting standard ranges, the participant should be provided with sufficient information to give meaning to the measurements taken, so that they may act on the results if necessary and arrange to see their general practitioner or other relevant health professional. In addition, based on predefined cut-off levels defined by a clinician, recommendations on actions due to deviations in biochemical tests and physiological variables will be given. Furthermore, if such deviation is defined as acute harmful, according to predefined limits, the participants will be contacted by e-mail and phone immediately from the test centre.

In normal healthcare settings, tests are conducted at the individual level immediately after sample collection; they search for specific conditions or outcomes; and, in the case of genetic tests, pre- and post-test counseling is provided. In EpiHealth, given the lack of knowledge at recruitment about the tests that might be done in this research context (and, hence, the inability to provide specific counseling beforehand), we will not in general provide participants with information (genetic or otherwise) about their own

individual results derived from examination of the database or samples by research undertaken after enrolment (with the exception specified below). Instead, the overall findings and implications of results that derive from EpiHealth will be made available to the wider community so that they can influence public health strategies.

However, there may be findings of new biomarkers implicating a very high risk of a preventable and serious disease. If such findings are made and corroborated, EpiHealth may contact individual participants to communicate these findings, if EpiHealth in agreement with relevant medical expertise finds this defensible. EpiHealth commits itself not to contact genetic relatives to communicate this kind of information.

4. Ongoing engagement with participants and the public

Regular communication will be important to inform participants of general findings from research based on the resource and to encourage continued participation. EpiHealth will therefore look for a variety of ways for communicating with (including listening to) participants, the general public, researchers and the scientific community. One such way would be by the EpiHealth home page where research results will be communicated both in a scientific way when the results have been published, but also in a manner that could be understood without skills in medicine.

5. Re-contact

It will be explained to participants that they will be re-contacted by EpiHealth for various reasons, including:

- To collect new information (such as questionnaire data, measures or samples) for the resource. It is anticipated that repeated questionnaires will be asked for every five years. A repeated re-examination at the test centre after 10 years would also be desirable, but are pending additional resources.
- To seek consent to proposed new uses that have passed scientific and ethics review but which do not fall within the existing consent.
- To ask participants whether they would be willing to participate in another study that requires new information or samples. It will be emphasized that participation in all such re-assessments is entirely voluntary.

Decisions on whether re-contact is appropriate for particular proposals will be made by EpiHealth and will be subject to a new Ethics Committee approval.

6. Right to withdraw

Participants will be advised at enrolment that they have the right to withdraw parts of or completely their consent to participate in EpiHealth and that this can be done at any time without having to explain why and without penalty. This is essential to preserve and demonstrate the voluntary nature of participation. During enrolment, EpiHealth will provide information to participants about the options for withdrawal of consent:

- **"Blood sample withdrawal":** EpiHealth will not use stored blood samples collected in the biobank.
- **"DNA withdrawal":** Epihealth will not use stored DNA collected in the biobank.
- **"Official registries withdrawal":** Epihealth will not merge collected data with official registries and national quality registries in order to gain the information specified in the EpiHealth information brochure.
- **"Medical records withdrawal":** Epihealth will not merge collected data with medical records.
- **"No further contact":** EpiHealth would no longer contact the participant or obtain further information from their health-relevant records in the future, but would still have their permission to use the information and samples provided previously.
- **"Complete withdrawal":** In addition to no longer contacting the participant or obtaining further information from records, EpiHealth will completely stop using any health-related information and samples collected previously. Such a withdrawal would prevent information about them from contributing to further longitudinal analyses, but it would not be feasible to remove their data from analyses that have already been done.

If a participant decides to withdraw then EpiHealth would seek written confirmation of the level of withdrawal from the participant.

EpiHealth website will post a short summary of approved study proposals one month prior to data/sample extraction thus enabling the subjects to evaluate the scientific development of EpiHealth and, if preferred, withdraw their participation in EpiHealth.

Participants will not be automatically withdrawn if they lose mental capacity or die. In all events, EpiHealth will continue to safeguard the confidentiality and security of all participants' data and samples as long as it holds them, including after a person's mental incapacity or death.

7. Expectation of personal financial gain

Participants will not be offered any material financial inducement to contribute to EpiHealth, irrespective of whether the use of data or samples might ultimately lead to profit.

8. Information security

EpiHealth is committed to protecting the confidentiality, integrity and availability of data and samples. This is achieved by implementing a set of controls, including policies, processes, procedures, organizational structures and software and hardware functions. All information security management measures are based on the SS-ISO/IEC 27000-standard.

EpiHealth needs to hold identifying information (such as name, address, birth date, personal identity number) to invite and handle participants and to allow follow-up of participants' health. All EpiHealth staff will be required to sign confidentiality agreements as part of their contracts.

II. Relationship with researchers

A. STEWARDSHIP OF DATA AND SAMPLES

EpiHealth will serve as the steward of its resource, maintaining and building it for the public good in accordance with its purpose. This implies both the judicious protecting and sharing of the resource. Participants will not have property rights in the samples.

As well as respecting the commitments made to participants in the consent agreement, EpiHealth will strive to build a relationship of trust with participants and the wider public, in order to foster acceptance of the ways the resource is developed and used.

EpiHealth is governed by the Steering Committee with representatives from Uppsala and Lund Universities.

B. RESEARCH ACCESS TO DATA AND SAMPLES

1. General principles of access

EpiHealth will retain full control of all access to, and uses of, the resource. Research proposals will be reviewed by EpiHealth Data Access Committee (EDAC) to ensure they are consistent with the participants' consent and this Ethics Policy document, and that they have relevant ethics approval. All users, whether employed by universities, government, charities, or commercial companies, will be held to the same scientific and ethical standards.

Exclusive access to the fully developed resource will not be granted to any party. Use of the biological samples will have to be carefully coordinated and controlled since they are limited. The general criterion for such a priority is the scientific and potential health value of the research projects in question, as judged by EpiHealth Data Access Committee.

2. Access to EpiHealth data and samples

The EpiHealth Steering Committee will have the overall decision-making authority over access to and use of the resource.

In cases of international researchers applying for access to EpiHealth resources, EpiHealth will act in accordance with the Swedish Biobank Act [chapter 4, §3] and

require a Swedish research institution to file for approval for sharing samples outside Sweden. All researchers (Swedish and international) need to sign a contract. Access to data and/or samples will be granted under license for scientifically and ethically approved research consistent with EpiHealth purpose.

3. Sharing of data and findings

EpiHealth seeks to augment the value of the resource in order to ensure that the greatest potential benefit for public health may be realized from it.

All researchers will be asked to deposit data and results from analyses made on participants' data and samples, and any relevant supporting information, in the EpiHealth database so that they are subsequently available to all researchers with appropriate scientific and ethics approval.

There will also be a requirement on researchers to place the findings (whether positive or negative) from research based on EpiHealth data/samples in the public domain so that people can benefit from them.

Researchers should acknowledge EpiHealth in publications, presentations, and patents filed.

III. EpiHealth governance and relationship with society

A. GOVERNANCE, MANAGEMENT AND ACCOUNTABILITY

1. Organization and management

EpiHealth has its origin in a collaboration project between Uppsala and Lund Universities sponsored by the Swedish Research Council (VR). As such, the EpiHealth Steering Committee holds representatives from both Uppsala and Lund Universities. It may well be in the future that the project expands also to other universities, which then will be represented in the Steering Committee.

2. Relation to Swedish Universities

At present, EpiHealth only include Uppsala and Lund Universities. However, EpiHealth aim to become a national Swedish resource for research, not only at Uppsala and Lund Universities, but all Swedish Universities. EpiHealth will thus seek and foster the best collaboration with other Swedish Universities and in particular the universities with medical faculties. EpiHealth has already a close collaboration with LifeGene at Karolinska Institute (KI) in terms of bioinformatics and biobanking.

EpiHealth will have a detailed strategy for handling contingencies in the event that EpiHealth has to close or make other substantial transitions in the holdings or control of the resource. The objective will be to ensure that the protection and respect for the rights of the participants provided by this Ethics Policy document continue to be maintained. Information about such measures will be made available to participants.

B. OPERATIONAL

1. EpiHealth Staff

Staff activities are carried out in accordance with the highest legal norms and ethical principles. All EpiHealth staff will be required to sign confidentiality agreements as part of their contracts. EpiHealth will ensure that all of personnel are knowledgeable about its goals and mission. Test center personnel will be trained in communicating the consent information and assessing the understanding of participants in order to make sure that participants understand what they are consenting to when they agree to take part. EpiHealth will employ professional and technical staff with the appropriate competency to operate the equipment effectively.

2. EpiHealth resources - data/biological samples

EpiHealth will ensure that it has appropriate staff and resources to preserve records, data, and biological materials appropriately, to handle requests for access to data and biological materials, and to operate efficiently in all aspects. Quality assurance measures will be in place, including conditions to ensure continued operation of storage, security and confidentiality during collection, storage, handling, distribution and destruction of the human biological materials and data. The Uppsala Biobank and Region Skåne Biobank or the Lund University biobank, as parts of the BBMRI.SE network of regional biobanking nodes, serve as a custodian of the biological samples and adhere to the Swedish Biobank Act and other regulations to protect the integrity of the donors. Also collaboration with the KI biobank has been established.

EpiHealth will be responsible for ensuring the security, confidentiality and custodianship of biological materials and data, including the implementation of adequate protection measures.

C. FINANCIERS/FUNDING

In order to ensure transparency, EpiHealth will publicly make available information on the financial model that it intends to adopt over its lifespan in order to ensure its sustainability. Where EpiHealth foresees attracting private or foreign investment or entering in commercial collaborations, this will be clearly articulated and communicated, especially to participants.

1. Character of financiers/commercial partners

Funding of EpiHealth may come from public, private, or public-private partnership sources. Any financier is allowed that will not by its presence or reputation risk to taint EpiHealth´s brand or counteract EpiHealth's purpose. It is important for EpiHealth to be perceived as a research resource aimed at public health and the public good, not a commercial enterprise or a source of information that may be shared for other purposes.

EpiHealth will not share individualized information with financiers/commercial partners. Even if such a financer would not receive information held by EpiHealth, the public may perceive this as a risk, making them less inclined to participate. EpiHealth will therefore consider this particular risk before allowing a new potential financer or commercial partner.

The approval of a financier or commercial partner will be based on the following criteria:

- Financiers are only allowed that will not by its presence or reputation risk to taint EpiHealth's brand or counteract EpiHealth's purpose.
- Financiers must not impede the possibility for EpiHealth to recruit and retain participants.
- Financiers must not be from areas of business generally regarded as morally questionable, such as tobacco or arms.
- Financiers must have an ethical policy approved by EpiHealth.

EpiHealth will have the right to dispense of financiers whose conduct is inappropriate for an EpiHealth financier. In such a case the financier will get the proportion of its resources that is left unused.

Co-branding such as the company using EpiHealth's logo in their own advertisement is not allowed. EpiHealth will be restrictive towards co-branding.

2. Commercial partnerships

EpiHealth is wholly a research resource for the public good. This means that individual researchers with approved projects can commercialize their results originating from the EpiHealth resource, but EpiHealth itself will not commercialize any results.

A commercial partner can interact with EpiHealth in several ways:

- As a general financier or a sponsor (see above).
- As a backer of a certain research project: for access to the EpiHealth resource they need the research project to be ethically and scientifically approved by

Regional Ethics Committees. EpiHealth will charge license fees from researchers and to get access to data and/or samples.

D. BENEFIT SHARING

1. Dissemination of knowledge generally

The purpose of EpiHealth is to learn from the collective health experience of the participants over time, in order to generate and disseminate new knowledge to benefit the health of the public in Sweden and elsewhere.

Knowledge derived from studies based on EpiHealth will be:

- Published in scientific and medical literature.
- Communicated to EpiHealth participants (by the web-site), the National Board of Health and Welfare and others (as appropriate).
- Knowledge derived from studies may also be applied to the development or improvement of healthcare techniques, technologies, materials or routines.

E. THIRD PARTIES

1. Ethics approval by relevant ethics committees

The core scientific protocol and operational procedures of the EpiHealth resource, as well as proposed uses of it, will have approval from appropriate Ethics Committees (i.e. from the Swedish Regional Ethics Boards), in accordance with guidance from relevant bodies and with relevant provisions. Participants will be told that such independent ethics approval will be obtained.

2. Third parties with non-research interests

There are many third parties, with an interest in genetic and other health-related information of the kind that will be part of EpiHealth's resource, who want to use the information for other purposes than research. Examples of such parties are relatives of participants, commercial companies, insurance companies, employers, healthcare authorities, police, and forensic authorities, to mention a few. By support from the

Genetic Integrity Act, EpiHealth will not disclose any information to these parties, no matter how persistent their demands.

However, if genetic information is fed back to a grown individual, insurance companies has the right to inquire for (from that individual) and use that information when selling, changing or renewing a personal insurance (health, life, or pension insurance), given that the amount of compensation exceeds a certain amount of money (30 base amounts as defined by law for compensations paid on one occasion and 4 base amounts for regularly paid compensations).

By court order there is a theoretical possibility that EpiHealth is enforced to provide de-anonymized information, primarily to authorities responsible for upholding the criminal law. Under such circumstances the final decision rests with the management of the universities.