LifeGene Ethics Policy

Version 3.2

LifeGene Ethics Group

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LifeGene - purpose and overview

LifeGene is a national collaborative project designed to build up a resource for research in all medical disciplines, enabling new and groundbreaking research on the relationships among heredity, environment and lifestyle. The LifeGene project will include studying half a million Swedes aged 0-45 with the aim of creating new tools to prevent, diagnose and treat our most common diseases. A pilot study is planned for 2009 and the roll-out of the project is planned for 2010.

In this Ethics Policy document, the ethical framework and standard of LifeGene is presented.

Half a million Swedes will be contacted for collection of information concerning their health, lifestyle and exposures, and donation of samples. LifeGene will be longitudinal with repeated contacts of study participants. LifeGene will seek active engagement with participants, research users and society in general throughout the lifetime of the resource. Data and samples will only be used for ethically and scientifically approved research consistent with the above purpose. Safeguards will be maintained to ensure the confidentiality of the participants' data and samples.

LifeGene will constitute a platform for a myriad of biomedical research projects. Researchers not only in biomedicine and biotechnology but also behavioral and social sciences may benefit from access to LifeGene. By combining a biological perspective with e-epidemiology, LifeGene will open up new possibilities for a greater understanding of the interplay between heredity, lifestyle and the environment as regards to our most common diseases, possibilities strengthened by the longitudinal aspects of the study. Exposures such as diet, physical activity, smoking, prenatal environment, infections, sleep-disorders, socioeconomic and psychosocial status, to name a few, will be assessed.

The data-sharing policy of LifeGene will conform to international recommendations. Key to the LifeGene effort will be modern bioinformatics and state of the art biobanking on all levels. The open-access resource will provide new information about the causes of diseases that holds a good chance of leading to their prevention, refined diagnostic methods and therapeutic opportunities.

I. Relationship with participants

A. RECRUITMENT

1. General principles

LifeGene aims to recruit 500,000 people aged 0-45 from all over Sweden. This must be done in a manner that respects the integrity of the participants. For LifeGene, the rights and wellbeing of the participants prevail over the research interest of LifeGene and its users. In order to ensure this LifeGene will adopt strict and well-established norms of transparency, accountability and consent in relation to its participants.

Regarding those who have reached their lawful age, LifeGene does not intend to enroll people who are unable to give consent (e.g. because of mental disability); those who are unable to take part in data collection (e.g. because they are too ill); or those who are uncomfortable with any of the conditions of participation. Staff will be trained to judge each potential participant's capacity to give consent and to take part in data and sample collection.

The recruitment of those who have not yet reached their lawful age (minors), is an especially sensitive issue since one cannot expect that they can understand and agree to the terms of participation themselves. In society in general, the parents (or other legal guardian) have the responsibility to act in the best interest of their minors and to decide on their behalf. Therefore, the consent of parents is a prerequisite for recruitment of minors in LifeGene until the time when the minor herself is considered able to decide for herself whether or not to participate. Due to the special care that has to be taken with the recruitment of minors, the relationship with this group is of paramount importance (see I.B.1).

Participation in LifeGene is voluntary. All aspects of recruitment, from initial contact with potential participants to enrolment at the baseline assessment visit, will be conducted in a way that preserves the voluntary nature of participation and respects cultural differences.

In order to generate scientifically valid results, LifeGene must also obtain agreement from participants for examination of the progress of their health in depth and over time. This means that LifeGene 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 re-contact and access to records, as well as termination of participation in the biobank at large should they choose. Again, this follows the line of voluntary participation in LifeGene.

LifeGene will act in accordance with the Personal Data Act and all other relevant legislation. Compliance with the Personal Data Act together with the Swedish Act on Secrecy and the Genetic Integrity Act is necessary to ensure the confidentiality of the participants in LifeGene. LifeGene will also seek all necessary approvals that are required for the planned invitation, assessment and follow-up procedures (e.g. from relevant ethics committees, the National Board of Health and Welfare and other relevant bodies). LifeGene will also require that all research projects gaining access to the biobank are approved of by the Independent Regional Boards of Ethics of Research in accordance with the Ethical Review Act. Although the Biobank Act does not strictly apply to LifeGene, since LifeGene does not collect samples in the health care context [chapter 1, §3], LifeGene commits itself to act in accordance with the higher standards of the Biobank Act. LifeGene will also comply with international conventions, such as the World Medical Association Declaration of Helsinki and relevant European international guidelines of European Society of Human Genetics (ESHG), Organization for Economic Co-operation and Development (OECD), and United Nations Educational, Scientific and Cultural Organization (UNESCO). LifeGene commits itself to continuous monitoring of and revisions in accordance with these and other relevant legislations, guidelines, and conventions. If there are discrepancies between these documents, LifeGene will respect domestic laws and beyond that conform to the principles with highest ethical standards. The monitoring will be done by LifeGene itself as well as by the independent LifeGene Ethics Council. Any participant experiencing that LifeGene has failed to fulfill its obligations towards her may turn to this Council.

2. Selection and approach

LifeGene will seek to recruit as widely a generalizable population sample feasible in order for the research to ultimately benefit as wide diversity of the population as possible. Although the focus of LifeGene is common diseases, no recruitment selection will be performed so as to target any specific diseases.

LifeGene will work to reduce barriers to participation (such as those relating to age, gender, sexual orientation, ethnicity, social class, residence, employment, language and illness) through, among other things, the location and opening times of assessment centers and by translation of information materials. Participants with disabilities, such as hearing impediments, will be given information through means adapted to their communication needs. LifeGene will also commit itself to respecting the cultural heritage and religious beliefs of the participants in collection of, use of and destruction of data and samples; given that LifeGene is made aware of any such implications of culture and religion from participants.

LifeGene will identify potential participants from official registries. These contact details will be processed in confidence by LifeGene in accordance with the Personal Data Act. Potential participants will then be sent information about the study and invited to attend a local LifeGene In Person Testing Center (IPT) or Assessment Center.

3. Enrolment

Potential participants will receive, by ordinary mail, information about LifeGene and an invitation to participate in the study. Further information will be available from LifeGene through a free telephone service and a website.

The invitation mail will include instructions on how to enroll on the web, by calling the LifeGene call-center or by using the mail provided in the invitation. During enrolment, which demands a pro-active activity from the participant, a *preliminary* consent will be signed (check-box on the web, recorded consent at call-center, written consent by mail) by the participant. During the Assessment Center visit the complete consent will be signed. Here LifeGene 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, pregnancies etc.) and other factors (such as cognitive function and medical history, etc.), executing physical measurements (e.g. blood pressure, size, weight, grip strength, lung function, etc.) and giving blood and urine samples. For certain sub-groups additional physical measurements and samples (e.g. saliva and feces) may be required.

B. UNDERSTANDINGS AND CONSENT

1. Consent

Consent will be sought to participate in LifeGene. 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 LifeGene's stated purpose.

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

- the purpose of LifeGene, 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 a 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 LifeGene as a research resource

- the fact that LifeGene will be the legal owner of the database and the sample collection, and that participants will have no property rights in the samples
- the kinds of safeguards that will be maintained, including secure storage of data and samples in reversibly anonymized form (as explained in Section I.C.2), and severe restrictions on access to data and samples that are not anonymized
- the assurance that only research uses that have been approved by both LifeGene and a relevant ethics committee will be allowed, and that data and samples will be anonymized before being provided to research users, [unless a court order demands that information be released to authorities (e.g. police), in which case LifeGene will appeal against this to the highest possible level of judicial institution
- the expectation that commercial entities and non-Swedish researchers will apply to use LifeGene and that commercial entities may obtain IP rights based on the results of their research
- the expectation of being re-contacted in the future by LifeGene and the purpose of such contacts as well as the expectation that other studies connected to LifeGene may initiate contact
- the right to withdraw at any time without having to give a reason and without penalty, and the meaning of different levels of withdrawal
- the circumstances in which healthcare information about individual participants may be fed back and the options to get such feedback
- LifeGene's commitment to maintaining active engagement with participants and society in general
- information about how to contact LifeGene in case of questions and where more information can be found

The points listed above are some elements of what it means to participate in LifeGene; each is discussed in more detail later in this document. These elements and other customary undertakings will be addressed in information provided to participants during the consent process.

As regards minors (age below 18), the consent of the parents (or other legally appointed guardian if not parents) must be obtained. Both parents, if there is more than one, will be informed in the initial contact, so that they can agree on how to consent. The signed consent of at least one parent is required and both parents will be informed about the option to withdraw consent. As a rule, from the age of 15, the child has a right to decline any further participation if he or she understands the nature and terms of participation in LifeGene. However, even younger persons may be able to understand the nature and terms of participation and thus to assent or resist participation. If parents to children below the age of 15 judge them to have this ability and the child or children in question wish to terminate their participation, LifeGene will respect this decision. Moreover, until

participants reach their legal age of 18, either parent always has the right to withdraw the participation of their children. When a participant reaches the age of 18, he or she should have the same rights as the participant that had reached lawful age at the time of initial consent. Consequently, they will be contacted at the age of 18 with the same information about participation as other adults receive, including how to withdraw consent. Note that no new signed consent is needed from the person reaching legal age. It is important to safeguard the privacy of children and to point out to parents that results about children obtained by LifeGene will not be fed back to parents to any larger extent than for adult participants in general (see I.B.3).

LifeGene will endeavor 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. An evaluation of the consent procedure will be conducted in preparation for the main phase of recruitment.

The consent to participate in LifeGene will apply throughout the lifetime of LifeGene unless the participant chooses to withdraw. New consent will be sought for any proposed activities that do not fall within the existing consent (see also I.B.5).

2. Collection of data from relevant records

The ability to accumulate data from relevant health-records will be essential for the success of LifeGene. LifeGene wants to track health events, the development of disease, and the course of treatments. Thus, LifeGene 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.

LifeGene 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, Emigration register, Multigeneration Register, Hospital Discharge Register, Outpatient visits register, Prescription Register, Cancer Register, Tuberculosis Register, Medical Birth and Malformations Register, Infectious Disease register and national quality registries e.g. RiksHIA). Access to such records, at least in some instances, as well as the establishment of LifeGene's biobank in general, will require the approval of The National Board of Health and Welfare. During the consent process LifeGene will explain to participants 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 LifeGene will collect psychiatric records has to be clearly defined, balancing the privacy of the individual and the interest of research.

LifeGene 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

LifeGene will aim to ensure that participants understand that enrolment does not provide them with a general health check. LifeGene is primarily a research endeavor and not a health care screening program in the clinical setting. For instance, at the IPT, personnel are not primarily physicians and do not have access to full medical records. As a consequence, the significance of the observations might not be clear and LifeGene staff would not be in position to interpret their implications fully. Further, it is not likely to be constructive, and might even be harmful (including causing undue alarm and having potentially adverse effects on insurance and employment status), to provide information without prior counseling or support. For these reasons, LifeGene will only provide some carefully considered individual health information to participants. However, it is possible to provide participants with the results of some measurements or observations at several occasions: at the IPT visit (e.g. blood pressure or incidental findings), from the front end analysis (e.g. red cell count, cholesterol level), and later as results arise from research studies (e.g. genetic or biochemical information).

What kind of results and what measurements that will be provided to participants are not defined at present. This has to be processed by LifeGene in collaboration with relevant medical expertise, e.g. from the Swedish Society of Medicine, which can provide the clinical experience needed. Furthermore, LifeGene has to collaborate with those likely to manage the participants who have received information potentially relevant to their health, i.e. the health care system. Any proposed feedback must therefore be supported by the relevant health care institutions. In Sweden, most health care institutions are on the regional and local levels. Thus, the support of SKL and other relevant institutions is of great importance.

The personnel providing the feedback must be trained professionals who are able to explain the implications for the individual regarding his or her health information. In the case of especially sensitive information with relevance for others, such as relatives, proper counseling is needed.

Specifically, provision of health information at the three stages will cover:

- **At the IPT visit:** Participants will receive some of the measurements taken during the enrolment visit (e.g. blood pressure, lung function, height, weight, estimated amount of fat), if so consented. Consequently, a printed report will be provided at the end of their visit as a means of feeding back such measurements. The data will also be available at a personal web-site for the participants. 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 GP or other relevant health professional. The legal duty of care for staff will be determined by the research context, and will apply mainly to safe and competent collection of questionnaire data,

measurements and blood or other samples. LifeGene will inform relevant health care institutions when the project is initiated about its existence and modus operandi. LifeGene staff should be able to recommend to participants where in the health care system they should turn in case of abnormal measurements or incidental findings.

- **Front end analysis:** Prior to storage of samples, LifeGene is planning to conduct routinely only few analyses in biological material, including investigations that cannot be done subsequently on stored samples (such as hematology). LifeGene will feed back some of these analyzes to participants, if so consented. By reporting standard ranges, the participant should be provided with sufficient information to give meaning to the analyses taken, so that they may act on the results if necessary and arrange to see their GP or other relevant health professional. Then, if needed, participants must receive proper and professional support and counseling regarding the implications of the findings either from LifeGene or LifeGene has to ensure this is received from a relevant health institution.

- **Later, as a result of research studies:** 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 LifeGene, 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 LifeGene will be made available to participants and the wider community so that they can influence public health strategies (including, where appropriate, the introduction of screening for newly discovered risk factors).

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, LifeGene may contact individual participants to communicate these findings, if LifeGene in agreement with relevant medical expertise finds this defensible. This will only be done provided the participant has agreed to be contacted with such information, since this would require de-anonymization of the participant. Such re-contact is made through inviting the participant to an individual counseling session with a professional counselor. The case handling will be performed in collaboration with relevant health care institutions. LifeGene 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. LifeGene will

therefore look for a variety of ways for communicating with (including listening to) participants, the general public, research users and the scientific community.

A variety of media, such as the LifeGene website, help-line, newsletters, and public meetings will be used to inform participants about the development and use of the resource, and of ways to contact LifeGene (including e.g. how to withdraw). Systems will be put in place to allow participants to indicate how, and whether, they would like to receive such information.

Each individual participant will obtain a password to his/her personalized page on the LifeGene homepage. Here the participant will be able to receive his/her information from IPT and questionnaires as well as other relevant information.

LifeGene may also establish a participants' panel with a clear remit that it is as representative as possible of the LifeGene population and able to express views typical of the participants generally. LifeGene will also maintain procedures for responding in a timely fashion to any enquiries or complaints.

5. Re-contact

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

- To collect new information (such as questionnaire data, measures or samples) for the resource. It is anticipated that repeat assessment visits would be done every five years. For representative subsets of people, especially children, sequential repeat assessments may be done more frequently. Invitations to provide additional information that do not require such visits (e.g. questionnaire data collected by mail or internet) will be sent to all participants more frequently during the study, probably on a yearly basis.

- 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 for researchers to contact them to discuss possible involvement in a study that requires new information or samples. It will be emphasized that participation in all such re-assessments is entirely voluntary, and that any initial re-contact not undertaken by participants themselves will be undertaken by LifeGene.

Decisions on whether re-contact is appropriate for particular proposals will be made by LifeGene and will be subject to Research Ethics Committee approval. When re-contacting special sub-populations, care will be taken over the use of selection criteria (such as genetic make-up) that might inadvertently reveal information to participants about themselves of which they may not be aware.

6. Right to withdraw

Participants will be advised at enrolment that they have the right to withdraw from LifeGene at any time without having to explain why and without penalty. This is essential to preserve and demonstrate the voluntary nature of participation. Should participants become incapacitated or die, they would no longer be able to withdraw themselves. If participants wish to have their information in any way inaccessible in such events, they must inform about this on beforehand.

When withdrawing, in addition to no longer contacting the participant or obtaining further information from records, LifeGene will completely anonymize data and samples collected previously. This means that it cannot be traced back to the individual in question; i.e. the digital key connecting data and samples with the individual will be deleted. Data already gathered may be used in the anonymized form for future research if applicable. If a participant decides to withdraw then LifeGene would seek written confirmation of the level of withdrawal from the participant. LifeGene will need to retain some minimal personal data for a number of reasons, which include: ensuring that participants who have withdrawn are not re-contacted; and assessing the determinants of withdrawal and any impact on research findings. Participants who withdraw will be assured that this administrative record will not be part of the main database that is available to others. Some administrative details (such as their signed consent and withdrawal) would also be kept as a record of their wishes, without the possibility of connecting these details to the data and samples.

Participants may have the possibility to limit their participation in two ways without withdrawing.

- **"No further contact":** LifeGene would no longer contact the participants directly, but would still have their permission to use information and samples provided previously, and to obtain further information from their medical records if they previously have consented to access of medical records.

- **"No further access to medical journals":** LifeGene would no longer obtain further information from their medical records in the future, but would still have their permission to use the information collected previously.

Despite LifeGene's efforts to stay in touch with participants, it may well lose contact with some as they relocate, emigrate, or do not respond to communications. Where a participant has not actively withdrawn, LifeGene will continue to use the samples and data and maintain linkages, although it will not be able to update some data (e.g. those collected by repeat questionnaires).

7. Expectation of personal financial gain

Participants will not be offered any material financial inducement to contribute to LifeGene, irrespective of whether the use of data or samples might ultimately lead to profit. Reasonable expenses incurred through participation (such as travel and parking)

will be reimbursed as required by the participant. As is explained in Section II.A, participants will be told that their involvement will not create or confer any property rights in samples.

C. CONFIDENTIALITY

LifeGene is committed to protecting the confidentiality of data and samples. Systems will be in place for secure data flow and for protecting confidentiality, (reversibly) anonymizing data and samples, and enforcing security. These measures will be explained to participants during the consent process. Some principles and comments on these matters follow in this section.

1. Commitment to maintaining confidentiality

LifeGene will maintain strict measures to protect confidentiality, and will ensure that data and samples are (reversibly) anonymized, linked and stored to very high standards of security. The same protection will be extended under contract for any handling or analysis of data or samples by third parties engaged to provide services necessary for developing the resource. Research users will only be given access to anonymized data and samples.

2. Anonymization

LifeGene will need to hold identifying information (such as name, address, birth date, personal identity number) to invite and handle participants. However, directly at enrolment (regardless of method of enrolment) a unique study identification number will be used instead of any personal identification. Furthermore, any collected information will be stored separated from participants' personal information, including the study identification number.

All identifying information will be held centrally by LifeGene in a restricted-access database that is controlled by senior LifeGene staff. Only a few people within LifeGene will have access to the "key" to the code for re-linking the participants' identifying information with their data and samples (i.e. "reversible anonymization"). It is necessary to retain this link with identifying information to allow follow-up of participants' health; to eliminate redundant data (e.g. duplicate cases); to verify correctness and completeness of data against original records; to establish correct linkages among databases; and to find specific data or samples if participants withdraw. All access and usage of the key between personal identification and data will be logged.

3. Re-identification

Access to the key code will be restricted to only those LifeGene staff who need it to allow proper linkage of follow-up data and for other necessary procedures. All LifeGene staff will be required to sign confidentiality agreements as part of their contracts.

Researchers will not be able to identify individual participants from the anonymized data or samples that are provided to them.

4. Security

A wide variety of measures will be taken to ensure the security of data, samples, the database and the information technology system in general. These include staff training and confidentiality pledges, physical and electronic controls on access to data, internet security, and physical security. This should prevent identifiable information from being used – inadvertently or deliberately – for any purpose other than approved research (see Section II.B.1 below).

II. Relationship with research users

A. STEWARDSHIP OF DATA AND SAMPLES

LifeGene 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. It also extends to the careful management of any transfer of parts or all of the database or sample collection, as is addressed in Section III.A.6 (Transfer of assets or closure). Participants will not have property rights in the samples.

LifeGene will explain the legal status of the database and sample collection to participants, and its committed role as steward of the resource. Even when this status is understood clearly, it is likely that many participants will continue to be interested to know how their data and samples are used; for this reason, among others, LifeGene will inform participants about uses of the resource (see Section I.B.4) and will guarantee the right to withdraw from participation.

As well as respecting the commitments made to participants in the consent agreement, LifeGene 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. A detailed Access and IP Policy for use of the resource has been developed and will evolve further in response to users, participants and the wider public.

B. RESEARCH ACCESS TO DATA AND SAMPLES

1. General principles of access

LifeGene will retain full control of all access to, and uses of, the resource. LifeGene will not proscribe any medical or other health related research uses at the outset. However, all proposals will be reviewed by LifeGene 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 because they are limited and depletable. While the resource is being developed, LifeGene may use the early data and samples to validate and improve methods of data collection and analysis. There will be yearly calls for research project proposals needing biological materials in order to prioritize the use of the biological samples. The general criterion for such a priority is the scientific and potential health value of the research projects in question, as judged by LifeGene advised by the International Scientific Advisory Board.

Access to the resource by the police or other law enforcement agencies will be acceded to only under court order, and LifeGene will resist such access vigorously in all circumstances.

2. Decisions on access and use

The LifeGene Board of Directors will have the overall decision-making authority over access to and use of the resource. In practice, the Board will delegate decisions on routine applications to the LifeGene Managing Director.

LifeGene will explain, to participants and the public, the policies and procedures for research access. An overall policy and detailed terms of access will be developed (i.e. the Access and IP Policy) which addresses fairness and transparency of decision-making, the handling of conflicts of interest and the prioritization of use of samples.

In cases of international researchers applying for access to LifeGene resources, LifeGene 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. International researchers will be held to the same standards as Swedish researchers regarding access and usage of LifeGene resources. All researchers (Swedish and international) need to sign a contract.

The LifeGene commits itself to act in accordance with this Ethics Policy and the IP and Access Policy, in order to assure others that the resource is being used in the public interest.

3. Licenses for specific uses

Access to data and/or samples will be granted under license for scientifically and ethically approved research consistent with LifeGene's purpose. Licenses will be for specific uses under strict terms and conditions in standard access agreements, including compliance with the consent given, the provisions of this Ethics Policy and other policies. Fees will be charged for licenses.

4. Sharing of data and findings

LifeGene 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 research users will be required to put data and results from analyses made on participants' data and samples, and any relevant supporting information, in the LifeGene database so that they are subsequently available to all researchers with appropriate scientific and ethics approval. A time limit for delivery of such result will be set. LifeGene will require results to meet a standard of quality for incorporation into LifeGene's database.

There will also be a requirement on research users to place the findings (whether positive or negative) from research based on LifeGene data/samples in the public domain so that people can benefit from them. Publication should be in the peer reviewed scientific literature whenever possible. LifeGene will also explore further strategies for dissemination of findings (such as through accessible electronic archives).

Researchers will only be permitted to keep results based on LifeGene confidential for a limited and reasonable period as described in the Access and IP Policy (for example, while they prepare papers for publication, file patent applications or otherwise pursue reasonable competitive advantage for their efforts). This policy will apply to all research users, whether non-commercial or commercial.

Researchers should acknowledge in publications, presentations, and patents filed LifeGene for being the resource they used or relied on. LifeGene will provide to researchers using its resources detailed guidance on the manner in which it wishes to be acknowledged. There is no requirement on researchers to acknowledge LifeGene's sponsors other than what is minimally needed for the publication, e.g. there might be a need to mention equipment suppliers in order for other researchers to be able to reproduce the data.

C. RESEARCH ACCESS TO LIFEGENE INFRASTRUCTURE

LifeGene may allow for other research projects to use LifeGene's infrastructure, such as the IPT centers or the Biobank storage and LifeGene laboratory facilities, since LifeGene builds a national infrastructure and this may be a prerequisite for getting the funding together. The project has to pass the ordinary ethics review, should be consistent with the Ethical Policy of LifeGene and do not interfere negatively with LifeGene's own operations (e.g. participant recruitment). This has to be determined on a case to case basis by the LifeGene Board since these projects risk to taint LifeGene's brand or disturb operations. Especially university driven projects are endorsed but also industry projects can be allowed. The projects are expected to be totally separate from LifeGene (not using the LifeGene logo or name, but only using some part of the infrastructure). Fees can be charged for this service, with the possibility of charges being higher for organizations that might be expected to derive financial benefit from their project.

III. LifeGene governance and relationship with society

A. GOVERNANCE, MANAGEMENT AND ACCOUNTABILITY

1. Board of Directors

At present, LifeGene has its base at Karolinska Institutet and is run by a steering committee. As of now it is not exactly defined what organizational structure LifeGene will have in the future. Therefore, the relations of accountability are not fully clear at this stage. Since LifeGene aims at ensuring transparency and trust, the organizational structure will be made available to participants, researchers and other interested parties. However, already at this point in time, some things are clear regarding LifeGene's internal structure.

LifeGene will be run by a steering committee or a board of directors. Although the composition of members of the board is presently not settled, consideration must be taken as to who will be represented in the board in order not to run the risk of compromising the independence and the public acceptance of the board.

The Board will adopt this Ethics Policy and be responsible for making sure that all LifeGene policies and activities conform to it. The Board will also assume responsibility for matters of corporate governance, including the management of conflicts of interest within LifeGene. The Board retains overall responsibility for the direction, management and control of LifeGene, but it delegates day to day management to the operational part of LifeGene. LifeGene will have certified accountants monitoring its economic transactions.

2. LifeGene Ethics Council

The LifeGene Ethics Council should be established in a way that enables it to operate independently of them and of LifeGene.

The remit of this Council includes: acting as an independent guardian of the Ethics Policy and advising the Board on its revision, e.g. in light of changes in the legislative or regulatory context; if needed reporting publicly on the conformity of the LifeGene project with the Ethics Policy; and advising more generally on the interests of participants and the general public in relation to LifeGene, whenever LifeGene seeks such advice. The Council is also a means of resource for redressing breaches of the Ethics Policy.

In pursuing its remit the Council will engage with, and render accounts to, a number of internal and external audiences. Internal dialogues will be with the Board of Directors, the LifeGene Managing Director and the financiers. External dialogues could be with participants, regulatory or government bodies, other interested parties, and the general public.

In order to be able to fulfill its remit, the LifeGene Ethics Council should be appropriately knowledgeable about LifeGene's continuing activities. It is hoped that effective communication will occur on the basis of mutual respect and cooperation.

Normally the LifeGene Ethics Council will communicate its reflections and criticism informally. If the Council is not satisfied with LifeGene's response, it could make a formal statement of concern or, if necessary, make a public statement that certain actions should or should not be taken. In the extreme, members of the Council could resign in protest and announce this publicly.

The LifeGene Ethics Council will work in an open and transparent fashion. This may be achieved in a variety of ways, such as through publishing reports of its discussions or holding public meetings.

3. Advisory Boards

LifeGene will also receive independent scientific guidance from the International Scientific Advisory Board, when LifeGene finds this appropriate.

4. Relation to Swedish universities

At present, LifeGene has its operational base at Karolinska Institutet. However, LifeGene is a national Swedish resource aimed to benefit not only Karolinska Institutet but all major universities (Karolinska Insitutet, Uppsala University, Lund University, Gothenburg University, Linköping University and Umeå University) in Sweden. LifeGene will thus seek and foster the best collaboration with the major Swedish universities to make the resource regarded and treated as a national common resource. Accordingly, e.g. co-branding with the major Swedish universities is encouraged. Therefore the LifeGene logo should be designed to fit the logos of the major Swedish universities.

5. Revision of LifeGene Ethics Policy

The Board of Directors, the LifeGene Ethics Council, the financiers and other interested parties (including participants and members of the wider public) may propose amendments or revisions of the Ethics Policy. In particular, the LifeGene Ethics Council could advise on outstanding issues, and may propose adjustments in response to new developments. Adoption of any amendment or revision will rest with the Board of Directors.

6. Transfer of assets or closure

LifeGene will have a detailed strategy for handling contingencies in the event that LifeGene has to close or make other substantial transitions in the holdings or control of the resource. This will address the possibility of partial or full transfer of the resource, whether elective or as a result of insolvent liquidation. 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. Adoption of the Ethics Policy

The Board of Directors will adopt this Ethics Policy and will be responsible for ensuring that all LifeGene policies and activities conform to it.

2. LifeGene Staff

Staff activities are carried out in accordance with the highest legal norms and ethical principles. Specific roles and chains of responsibility of those involved in the LifeGene activities will be clearly delineated. All LifeGene staff will be required to sign confidentiality agreements as part of their contracts. LifeGene will ensure that all of personnel are knowledgeable about its goals and mission. The LifeGene Managing Director should ensure that all involved personnel have the appropriate professional qualifications that meet recognized standards, underpinned by experience, education and training and are assigned responsibilities commensurate with their capabilities. LifeGene will ensure recruited IPT personnel are 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. LifeGene will employ professional and technical staff with the appropriate competency to operate the equipment effectively. In light of the importance of ensuring appropriate and up-to-date knowledge of staff, training should be carried out in line with the frequency required by applicable domestic law and taking into account international legislation, regulation and practice. Training should form an integral part of LifeGene's quality system and should be part of the quality manual. Technical staff should be responsible for implementation of policies and procedures as established by the managing director of LifeGene.

3. Data Gathering

LifeGene should have a clearly articulated policy in regard to the selection of specimens to be gathered. The types of human biological materials and data collected and stored in

LifeGene should meet specified criteria justifiable based on the scientific objectives and purposes of LifeGene.

LifeGene should have a policy on how to deal with analysis that becomes possible or data that may be collectible in the future as a result of technological developments, especially if a new consent might be needed.

Protocols should be in place such that the least invasive approach, associated with the least physical risk to the participant, is pursued. Means to minimize the risk of invasive procedures has to be adopted.

4. LifeGene resources - data / biological samples

LifeGene will ensure that it has appropriate staff and resources to preserve records, data and human biological materials appropriately, to handle requests for access to data and human biological materials, and to operate efficiently in all aspects. When establishing LifeGene, consideration will be given to future collaboration and cooperation, especially as regards database compability and interfaces. Appropriate design elements providing for such compability and interfaces should be incorporated when creating the databases. LifeGene will give consideration to using standardized approaches for the collection, storage and analysis of human biological materials and/or data so as to facilitate cross-HBGRD data exchange and sharing. 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.

Confidentiality: See Section I.C.

Security: See Section I.C.

Accountability: LifeGene will have a responsible position or positions for ensuring the security, confidentiality and custodianship of human biological materials and data, including through the implementation of adequate protection measures.

Standard of procedures: LifeGene will develop and maintain clearly documented operation procedures and policies for the procurement, collection, labeling, registration, processing, storage, tracking, retrieval dissemination, use and destruction of specimens and/or data. The policy should take into consideration cultural heritage and/or religious beliefs known or disclosed by participants, and their representative groups.

Sustainability: LifeGene should have plans for ensuring the ongoing support of the human biological materials and data throughout its existence.

Traceability: All of LifeGene holdings should be maintained through a system that allows the administrative data, the human biological materials, the phenotypic data and any other information to be tracked. LifeGene should ensure traceability of the human biological materials and data in order to safeguard the participant's right to withdrawal.

Accreditation/Quality: All human biological materials and data should be subject to proper quality control and quality assurance measures at every stage of its processing including procurement, collection, labeling, registration, storage, tracking, retrieval, dissemination, use and destruction in order to ensure high standards of quality in all LifeGene holdings. Results from research carried out using human biological materials or data accessed from LifeGene should be incorporated into LifeGene and LifeGene needs to ensure these adhere to an adequate standard of quality applicable for incorporation. In order to foster the interoperability of systems and facilitate the scientific exchange of data and human biological materials, LifeGene will collect, process, handle and store the specimens and data in a manner consistent with internationally accepted technological standards and norms. Accreditation will be sought at SWEDAC.

C. FINANCIERS / FUNDING

In order to ensure transparency, LifeGene will publicly make available information on the financial model that it intends to adopt over its lifespan in order to ensure its sustainability. This could, for example, include information on the business plan both for the short term (e.g., for 5 years) as well as more long term planning. The nature and source of LifeGene's financing/funding has to be explicit and transparent. Where LifeGene foresees attracting private or foreign investment or entering in commercial collaborations, this will be clearly articulated and communicated, especially to participants. LifeGene will have a business strategy in the event that funding is terminated or its nature changed.

1. Character of financiers/commercial partners

Funding of LifeGene 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 LifeGene's brand or counteract LifeGene's purpose. It is important for LifeGene's image 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. Investigations into the incitement of participation show that such an image is important to make people inclined to participate.

LifeGene will not share individualized information with financiers/commercial partners that may have an interest in the information stored by LifeGene. Even if such a financer would not receive information stored by LifeGene, the public may perceive this as a risk, making them less inclined to participate. LifeGene will therefore have to, on a case by case basis, 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 LifeGene's brand or counteract LifeGene's purpose.

- Financiers must not impede the possibility for LifeGene 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 LifeGene.

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

2. Financier's rights

Financiers should have certain well defined rights. A logo on LifGene's homepage and right to use LifeGene as an example of their social responsibility, e.g. gold sponsor, is allowed if approved on a case to case basis by the LifeGene Board. Other co-branding such as the company using LifeGene's logo in their own advertisement is not allowed. LifeGene will be restrictive towards co-branding and different kinds of co-branding have to be discussed and approved by the LifeGene Board in order to determine exactly where to draw the line. A financier will not have right to more data than what is publicly available.

3. Financing in kind

Apart from monetary financing, provision of equipment, consumables, free use of resources (e.g. space for IPT or electricity) is accepted. If a company provides LifeGene with some equipment/consumables it is not by this entitled to data generated through that equipment. Here, the same rule applies as for all other projects that want access to LifeGene data, i.e. the project has to be ethically and scientifically approved by regional ethics committees.

4. Commercial partnerships

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

A commercial partner can interact with LifeGene in several ways:

- As a financier or a sponsor (see above).
- As a backer of a research project: for access to the LifeGene resource they need the research project to be ethically and scientifically approved by regional ethics committees. LifeGene will charge license fees from researchers and to get acces to data and/or samples.

- Commercial companies are allowed as an outsourcing partner if LifeGene can guarantee that the quality of service and confidentiality conforms to a high standard and is consistent with this Ethics Policy. The outsourcing partner should not by its presence or reputation risk to taint LifeGene's brand or counteract LifeGene's purpose. Also, LifeGene has to carefully consider whether an activity is suitable for outsourcing or not in light of LifeGene's public image.

5. Revenue from operations

Fees will be charged for access licenses (see Section II.B.3) and services (see Section II.C) to researchers with the possibility of higher charges for commercial enterprises. All income that LifeGene secures through fees or intellectual property rights will be reinvested in the resource or used to balance costs for LifeGene.

D. BENEFIT SHARING

1. Dissemination of knowledge generally

The purpose of LifeGene 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 LifeGene will be:

- Published in the world's scientific and medical literature.
- Communicated to LifeGene participants, the National Board of Health and Welfare and others (as appropriate).
- Accumulated and made available by LifeGene as a resource for further research (e.g. via archives of the findings of studies).
- Knowledge derived from studies may also be applied to the development or improvement of healthcare techniques, technologies, materials or routines.

2. Intellectual property, income generation and royalties

Intellectual property and access policies are being developed to help ensure that the LifeGene resource is accessible to all *bona fide* research users, but is not exploited improperly or used in any way that inappropriately constrains use by others. Terms of access will be embodied in legal agreements that reflect LifeGene's objectives.

LifeGene is not expected in itself to lead to patentable inventions that return significant income either to researchers or LifeGene, but it is expected to become a valuable common resource for research. Nevertheless, there is some chance that research conducted using the resource (which might be conducted by researchers in the public or

commercial sector, as well as the academic and charity sector) will subsequently support the development of an invention that returns a profit. As long as the research project using LifeGene's resource is approved in the standard manner, filing for IP rights by Swedish or international researchers is allowed. Participants will be informed about this possibility in the informed consent.

The biotechnology and pharmaceutical industries can play an important role in realizing health benefits in a practical sense by developing and improving the use of biomedical products. Commercial companies and other research endeavors that stand to make a profit will, therefore, be allowed access to LifeGene if their proposal falls within the LifeGene purpose and complies with the usual scientific and ethics requirements.

E. THIRD PARTIES

1. Ethics approval by relevant ethics committees

The core scientific protocol and operational procedures of the LifeGene 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 LifeGene'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 of the most conspicuous ones. By support from the Genetic Integrity Act, LifeGene will not disclose any information to these parties, no matter how persistent their demands. If, contrary to expectation, such demands will be made LifeGene will emphasize that the information in LifeGene's databases is anonymous and cannot meaningfully be interpreted and that it would be contrary to the law and LifeGene's commitment to its participant to de-anonymize this information.

However, if genetic information is fed back to a grown individual, insurance companies has the right to inquire for 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). This will be clearly stated in the consent. If a participant does not wish to take any risk regarding her personal insurance, he or she should decline the option to get feedback.

By court order there is a theoretical possibility that LifeGene is enforced to provide de-anonymized information, primarily to authorities responsible for upholding the criminal law. If this would be the case, LifeGene will resist such access vigorously in all circumstances and appeal for the continued right to non-disclosure to the highest possible judicial authority.