European Nutrigenomics Organisation (NuGO)
Bioethics Guidelines on Human Studies
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This document is the print version of the Guidelines and General Principles.

There you will find additional information like references, bioethics courses, or user's comments on the guidelines.

In addition, we invite you to get involved - the online tool allows you to express your views, experiences, additional information, etc. in order to enhance the guidelines.

Please also visit the online version under http://nugo.dife.de/bot/
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NuGO Bioethics Working Group

- Manuela M Bergmann bergmann@dife.de (German Institute of Human Nutrition, Potsdam-Rehbrücke (Germany), Department of Epidemiology)
- Marek Bodzioch (The Jagiellonian University (Poland), Medical College, Department of Clinical Biochemistry)
- Luisa Bonet (University of the Balearic Islands, Palma de Mallorca (Spain), Laboratory of Molecular Biology, Nutrition and Biotechnology)
- Catherine Defoort (UMR INSERM (France), Faculté de médecine Timone, Marseille, France, UMR INSERM-476)
- Georg Lietz (Newcastle University (UK), School of Clinical Medical Sciences, Human Nutrition)

Experts involved in the generation of the NuGO Guidelines

- David Castle (University of Guelph, Ontario, Canada)
- Anthony Cutter (Lancaster University, UK)
- Eve-Marie Engels (Eberhard-Karls-Universität Tübingen, Germany)
- Givi Javashvili (Member of the Council of Europe Steering Committee on Bioethics)
- Henriette Roscam Abbing (University Utrecht, The Netherlands)
- Ulf Görman (Lund University, Sweden)
Preface

The enhancement of knowledge in the field of nutrigenomics research aims at the well-being and quality of life of humans and the prevention and treatment of conditions by diet. This kind of knowledge can only be achieved by using human biological material in large numbers.

As part of its work on setting standards and establishing guidelines for nutrigenomics research, the European Nutrigenomics Organisation (NuGO) has developed the present bioethical guidelines for those engaged in human nutrigenomics studies.

All guidelines focus on human research and were set up according to international rules for which a consensus among European countries was achieved and documented. The guidelines apply to nutrigenomics research that:

1. involves an intervention on a person in the context of a research project (e.g. randomized trial with supplements);
2. uses biological material that has been or is to be removed to be stored for research uses;
3. uses biological material that was removed for a different purpose, i.e. other than 1 or 2 (e.g. left over tissue from medical treatment)

The NuGO guidelines do not constitute a legal text. In any case, research involving humans needs to be subject to domestic ethical approval which will have to be guided by the domestic law and the rules offered by the domestic ethical committee. The NuGO guidelines give general advices that may be used in the context of ethical approval, already during the phase of study design, or for education. By their application, human nutrigenomics research ethics will be standardized throughout the scientific community.
General remark
The freedom of research is necessary for the progress of knowledge and the society as a whole. Nevertheless, for any research involving humans, the overall principle is that the interest and the welfare of a person that volunteers participating in a study shall prevail over the sole interest of science [Convention on Human Rights and Biomedicine Article 2; Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, Article 3]. This implies that the evaluation of risks and benefit should always be an important issue: that all reasonable measures are to be taken to minimize risk and burden, and that risks should not be disproportionate to the potential benefits of the research activities. The application of the rules and procedures of good medical practice also during research generally guarantees the risks to be minimized.

Citation
The NuGO Bioethics Guidelines on Human Studies:
http://nugo.dife.de/bot/index.php
Oslo, September 17th, 2007
Informed consent

General principles

- Human studies including collection of samples, genetic and other data are only carried out after the research volunteer has given free and informed consent.
- A human study involving research volunteers who are not able to give informed consent can only be carried out if it is for their direct benefit. In this case, the consent must be given by a legal representative (guardian). However, the participant should be involved in the decision making process. Exceptionally, research with no direct benefit may take place under the condition that this kind of research cannot be carried out on individuals who are capable to give consent and no objection was made by the individual; authorisation has been given by the legal representative, and the research entails only minimal risk and minimal burden for the research volunteer concerned. [Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, Article 15-1, ii, iii, iv and v; 15-2 and 15-3]
- The participant has the right to withdraw the consent at any time without any consequences.
- Information and consent must be documented
- If storage of samples is planned, the consenting process should include the biobanking aspects (see Guidelines 8, 9, 10, 11, 12, 13, 14, 15)

Relevant documents

[2] Protocol on Biomedical Research
[50] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin

Guideline 1: Information during consent process

Information should be provided to the research volunteer in an adequate and comprehensive manner and should be documented. It is preferable to seek advice of experts in social sciences and communication, i.e. sociologists or psychologists, to optimize the information process.

The consenting process has to assure the participant understands:

- him or her being asked to participate in a nutrigenomics research project
- the voluntary nature of participation
- the differences between research and medical treatment and the limitation of the personal benefit
- necessary commitments arising from the participation in the research project.
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Topics to be covered:

• the overall plan of the project (study design, sampling, sample and data processing)
• a statement whether repeated contact of the research volunteer with the study team is envisaged
• the purposes, nature, extent and duration of the proposed use of the samples, including the possibility of genetic analyses
• the form of data storage and linkage for analysis (see Definitions: Anonymized, unlinked, Identified, coded, linked, see Figure 1)
• the fate of samples and data when the study is finished, the consent is withdrawn, or participant dies
• a statement whether the sample will be stored after the study has finished; if stored, information should be given on possible further use and the research volunteer’s right in that respect
• the research volunteer should have the possibility to indicate beforehand on a consent form the choices and restrictions on the use of his/her biological material [Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin, Article 21], see Restrictions
• possible risks involved in the participation (medical, social, legal)
• opinion of the Ethics Committee
• where applicable: rights and safeguards prescribed by law for the protection of those who are not able to consent to research
• right to withdraw authorization at any time without being subject to any form of discrimination particularly regarding medical care
• the form in which research and test results will be communicated, which is of particular importance if the test results could be linked to the research volunteer’s identity
• whether or not payment of expenses (e.g. reimbursement of costs for transportation) will take place
• circumstances under which the research volunteer will be re-contacted to renew the consent or circumstances under which no renewal of consent would be necessary for further research
• expected benefits of the research on the individual and societal level
• where applicable, any commercial prospects of the proposed research (including the possibility of filing patent applications on the results)
• in case of unlinked anonymization, the research volunteer needs to be informed that he or she can’t make use of his or her right to know or not to know genotype information (unlinked, see Figure 1, see Figure 2).
• the extent of, and conditions for, the possible transfer of samples and data to a third party outside the institution e.g. in the framework of multi-centric studies (anonymized or coded only; see Figure 1)
• the voluntariness of participation
• the right to withdraw consent without any penalty
Informed consent is considered a process of communication between researcher and participant which starts before the research volunteer is recruited into the study and prevails during the ongoing study in an appropriate manner. There should always be enough space for answers to questions that might arise throughout the course of the study. In every study the participant should have a phone number and a name of a responsible research volunteer who could be contacted in case any question arises.

Relevant documents

[50] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin

Guideline 2: Content of the consent form for a nutrigenomics study

The signed consent form serves as a record of the information conveyed to the participant and documents the individual having agreed to participate in the study.

It should therefore either include or refer to the information sheet giving all information mentioned in Guideline 1 and also the following statements:

- the research volunteer has read and understood the information sheet of the study
- the research volunteer had enough time to read the information sheet and the opportunity was given to ask questions.
- the participation is voluntary
- the research volunteer is free to withdraw consent at any time, without giving any reason, and without medical care or legal rights being affected
- the research volunteer agrees to take part in the study

Where appropriate, the following aspects are recommended to be included in the signature form (optional):

- the research volunteer understands his/her sample being used for genotype analyses
- options to what extent the research volunteer wants to be informed about the test results (not applicable if it is not planned to disclose test results individually)
- permission to use medical records or other sources of medical information (e.g. cancer registries)
- interest in participation in further nutrigenomics studies

Guideline 3: Informed consent for research involving research volunteers who are not able to consent

The process of obtaining informed consent should be adapted to the comprehension of the
research volunteer who is not able to give informed consent and must take place under the
presence of at least one witness (preferably next of kin or guardian) who is legally authorized to
sign the consent form.

If the volunteer is an incapable adult, possible previously expressed wishes or objections should
be considered. If the volunteer is a child, his or her opinion should be taken into account
depending on age and maturity. In any case, reluctance of the research volunteer should be
respected.

Guideline 4: Informed consent for biobanks

The collection of biological material and of personal data from an individual, including the routine
samples obtained within a medical or health care setting, must be subject to the donor’s
consent. Different consents are required for

• the collection of the sample
• its use in a specific research study
• its use for other research purposes
• its use by a third party
• its use in a commercial application or by a commercial partner

Guideline 5: Extent of informed consent for biobanking

The scientific potential of a collection of samples and data in a bio-repository is dependent on
the flexibility of its use in research. In this regard, the following two aspects are relevant:

• duration of storage of samples and data
• definition of the research scope for which permission for use of samples and data is
  granted

Permission of use for an unlimited time within a defined research scope is preferable. Under the
circumstance of such a timely unlimited consent, the research volunteer should be informed on a
regular basis about research that is being conducted using his or her sample, so that he or she
can effectively exert the right to maintain or to withdraw the consent.

A relatively broad definition of the research scope is preferable, i.e. that the consent form refers
to groups of genes related to particular pathways or states of health or diseases rather than to a
list of specific genes or a particular disease. Adhering to this strategy may obviate the need of
renewal of consent for new studies that are within the scope of the original study. However,
ethical approval by the domestic ethical committee is necessary in any case.

In cases where the scope of a study is different from the one the research volunteer had agreed
to, the volunteer has to be re-contacted and a new informed consent has to be obtained. If the
contact to the research volunteer can’t be made with reasonable efforts, the biological material should only be used after an independent evaluation considering the following aspects [Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, Article 22-1]:

- importance of the research question,
- aims cannot be achieved using biological material for which consent can be obtained,
- no evidence exists that the research volunteer has opposed to that particular research use.
Genotype Information

General principles

- There must be no discrimination or stigmatization of a person based on the genetic heritage. Nutrigenomics researchers should be sensitive to the potential problem of stigmatization and should seek advice of experts in social sciences and law where appropriate.
- Genotyping that will allow predicting high disease susceptibility is only acceptable to be disclosed in a research context if it is subjected to appropriate genetic counselling.
- The right to respect private life, as stated in the Article 8 of the European Convention on Human Rights and Fundamental Freedoms, implies the right to know any information collected on one person's health. Wishes of individuals not to be informed should be respected.

Relevant documents

[4] Universal Declaration on the Human Genome and Human Rights

Guideline 6: Disclosure of genotype test results

The extent, form, and timing of the disclosure of genotype test results should be consistent with what was agreed upon in the informed consent (see Guideline 1 and Guideline 2). It should be recognized that disclosure of test results on an individual level is not possible if samples and data are stored unlinked anonymized (see Guideline 1).

Genotype results attained during nutrigenomics research should preferably be communicated (see comment General information to be provided to the participants) to the research volunteers on a study group level, and should not be disclosed individually for the following reasons:

- solid evidence linking specific gene polymorphisms to the development of diet-sensitive pathological conditions or responses to dietary interventions is scarce;
- the phenotypic outcome of the kind of genotype data expected to be attained in the context of nutrigenomics research can be modified by many factors, making it very difficult (here the link to difficult) their interpretation, in terms of health benefit/risks to the participant, on the individual level
- communication of individual results in large-scale epidemiological research projects would convert the nature of the exercise from a research one into a mass screening undertaking, which might have quite different budgetary and counselling implications [Draft Report on Collection, Treatment, Storage and Use of Genetic Data, commentary to
However, if a research volunteer personally insists on receiving his or her personal test results, the information should be given emphasizing possible implications for him or her (see Guideline 7).

Researchers should seek the advice of their ethics committee of reference on the disclosure issue, on a case by case basis, whenever, in the course of nutrigenomics research, genotype information not originally intended to be obtained arises which might be of clinical relevance for the research volunteer or his/her relatives according to the current established knowledge.

Relevant documents

[54] Draft Report on Collection, Treatment, Storage and Use of Genetic Data

Guideline 7: Disclosure of genotype test results on an individual level

Whenever the disclosure of individual genotyping data is considered, the research volunteer concerned should be offered comprehensive information about the implications or possible outcomes of knowing genotype test results. If genotype test results are to be disclosed, the following aspects are relevant:

- Disclosure should be made by an appropriately qualified specialist in a personal communication that encourages the volunteer to ask questions and is adjusted to his/her level of comprehension. The specialist should also have specific counselling skills.
- The research volunteer concerned should also receive the genotyping results in written form containing sufficient information for the treating physician or any other relevant health care professionals.
Biobanks

General principles

• The establishment and the use of biobanks have to balance out the main ethical principles of freedom of research, which is necessary for the progress of knowledge, and the respect of human dignity and self-determination.

• The collection, storage and use of human bodily substances and data must be subject to the research volunteer’s consent which is based on information and voluntariness.

• Research volunteers must be protected by an obligation of privacy on all parts concerned with the establishment and use of biobanks.

• The generation and operation of the biobank must be subject to quality assurance measures.

Relevant documents

[ 3 ] Biobanks for research
[ 2 ] Protocol on Biomedical Research
[ 50 ] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin
[ 7 ] Research ethics guidelines for using biobanks, especially projects involving genome research
[ 54 ] Draft Report on Collection, Treatment, Storage and Use of Genetic Data, Working group of the IBC on genetic data
[ 56 ] Human Tissue Act 2004

Guideline 8: Ownership and governance

Agreements on the ownership of the samples and associated data should be established prior to biobanking and should be subject to multi party contracts. Usually the institution is the owner of the biobank and the scientist/principle investigator (PI) in charge of the biobank is the curator. As such he or she has to take all appropriate steps to protect the samples and data, its storage, use and access. All steps should be guarded by an independent data protection officer. The data protection officer must be appointed specifically by the institution and is responsible for ensuring compliance with the legal requirements applicable to the handling, sharing, or pooling of personal data.

The use of biobank samples and data by a third party should be subject to a research contract involving a consortium agreement. The contract should also cover the issue of patenting rights in
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Biobanks

Guideline 9: Storage of samples and data

Banking of directly identified (nominal) samples is unacceptable, as it offers little protection for preserving privacy. Personal identifiers should therefore be removed from the sample and data collected as soon as possible. However, it would generally be essential for nutrigenomics research to potentially be able to trace individuals. This can be achieved by coding the biological material and for the code key to be stored separately. Strict rules for storage and the use of the code key must be established.

Guideline 10: Independent review of research using materials stored in a biobank

The ethical review procedures for the use of material and data from a biobank generally may be adapted to the nature of the research and the extent to which the research volunteer concerned could be identified from the biological materials or associated data.

However, prior to the conduct of a research project involving the use of biobank samples and data, an independent review should always be conducted.

It is essential where:

- the project calls for linking the samples to identifiable data
- bodily substances and associated data are to be transferred to external researchers.

The use of biobank samples and data where the research volunteer is traceable in research is not within the scope of the original consent should require renewal of the informed consent.

Nutrigenomics pilot studies using unlinked anonymized materials from a biobank may be exempt from comprehensive ethical approval [Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin, Articles 21-25]. However, even if samples are unlinked anonymized, it must be verified that the research volunteer had not opposed to the kind of research intended (see also Guideline 1). Information on potential objection to a particular research may be kept coded together with study records or data files.

Relevant documents

[50] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin
Guideline 11: Benefit sharing

Generally, by international law [Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin, Article 7], the donation must not be paid for, although travel expenses can be reimbursed (see Guideline 1).

Individual research volunteers ought not to benefit financially. There are two reasons for this:

a. an ethical background: a human body and its parts are not for sale and

b. a legal background: to avoid exploitation of an individual.

In addition, the application of financial incentives is against the rule of complete voluntariness because it may put a stronger pressure on socially disadvantaged.

Benefit sharing must take place on the societal level. Financial gain from this kind of research should be re-invested in further research, welfare, or other.

Relevant documents

[50] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin

Guideline 12: Fate of the sample and associated data if consent is withdrawn

Withdrawal can relate only to identified or coded samples and data. In case the volunteer withdraws his/her consent, he/she should have the right to decide whether samples should be unlinked anonymized or obliterated. Research volunteer should be advised to take into consideration the importance of keeping materials within biobanks and explained that, alternatively to their obliteration, materials can be unlinked anonymized by stripping off all identifiers permanently (see Guideline 1). If the volunteer did not explicitly request the obliteration of the sample, the researcher may retain sample unlinked anonymously. The same is true for study data about the volunteer collected so far. Generally, it is preferable to keep the data unlinked anonymized unless the volunteer do not insist explicitly on deletion.

Guideline 13: Samples from deceased persons

Bodily substances from deceased persons can be extremely valuable to nutrigenomics research, i.e. nutrient composition of bodily tissues in relation to genotype. It ought to be possible to use data and biological material from deceased. They can be collected and recorded for biobanks and subsequently used in research on the same conditions as for living research volunteers. If the deceased has not given consent during his lifetime, the next of kin or another legally
authorized person can furnish it, provided that this is not inconsistent with the deceased's wishes as expressed during his lifetime. In any case ethical approval should be obtained.

Relevant documents
[3] Biobanks for research

Guideline 14: Quality control

Biobanks should have a quality assurance protocol (standard operation procedure, SOP). This should include systems for storage, coding (identification and preservation of anonymity) and registration. They must also have clear conditions for responsibilities and management including alerts in case the storage system fails, for backups of data files etc. The documentation about procedures of sample collection and preparation should also be attached to the SOP.

Guideline 15: Potential legal successor in case the hosting institution closes down or the responsible scientist is not working for the biobank anymore

Whenever transfer of an entire biobank is being considered, the scientists and institution involved should seek the advice and approval of an ethics committee. In principle, if the biobank is transferred to an equivalent institution:

- Transfer of already unlinked anonymized data and samples should be possible without any restriction. However, this has to be subject to independent review as well, to ensure that the recipient institution is able to maintain the biobank according to established standards.
- In case of traceable samples and data, unless the research volunteer has given consent to a potential transfer of the sample to an appointed institution, research volunteers must be contacted to obtain specific consent for the transfer.
- If the research volunteer cannot be contacted after a reasonable amount of effort, the biobank should have policy rules on how to proceed in such situations. The rules should be made known to the research volunteer who donates material to the biobank so that he/she can make up his/her mind beforehand. (Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin, Article 19-3)
- The research volunteer’s previous wishes, if any, should be followed.
- The transfer and closing procedures must be monitored by an independent body.

Relevant documents
[50] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin
Use and exchange of data and samples

General principles

- It should be recognised that Biobanks are distinct from collections of biological material in that their samples are associated with personalised data. A sample collection is mostly set up for a specific purpose or objective and is not dynamic in the sense of up-dating information on the research volunteers concerned. Both are nevertheless governed by the same general rules [Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin, Article 17]
- For thorough utilization of the scientific potential of biobanks, access should be granted to as many research workers as possible.
- Researchers who have contributed preliminary work of their own to the establishment of a biobank should be accorded priority of use for a certain period.
- Although open access is the principle, this should be decided on a case by case basis. All research projects using stored biological material and data should be subjected to scientific and ethical review (see Guideline 10)

Relevant documents

[50] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin
[3] Biobanks for research
[8] Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services
[4] Universal Declaration on the Human Genome and Human Rights
[9] Proposal for an instrument on the use of archived human biological materials in biomedical research
[2] Protocol on Biomedical Research

Guideline 16: Access to biobanks

Access to the biobank and use of its samples and data by third parties should be subject to stipulations in form of research contracts and should also be subject to full records for future reference. Access to information or samples for genetic research should be restricted to qualified investigators and subject to institutional oversight. The curator should have the responsibility of control over the access to the collection. Funding bodies of the biobank need to determine the purpose of the collection and if it is available to both commercial ventures and academic researchers. For large genetic databases, establishment of independent oversight bodies is recommended.
Guideline 17: Disclosure of personal data

Names, date of birth and addresses must not be transferred to a third party. Further objections of research volunteers have always to be respected.

Under exceptional circumstances which will have to be justified, personal data can be transferred if

- the individual consented to this transfer
- the data protection measures are as strictly followed by the receiver of the samples and data as by the primary holder

Guideline 18: Use of biological materials and data in further research projects

Secondary use of stored biological material, in the context of these guidelines meaning the study aim differing from the original one, should always be subject to ethical approval. Where data and samples are not unlinked anonymized, consent should be renewed if possible with reasonable effort (see Guideline 1, Guideline 5). All information and communication tools such as advertisement, mailing, inquiry to registries etc. should be used to trace the research volunteer concerned. However, if expenses are disproportionately or if the donor is dead the effort for renewal of consent would be unreasonable. In those cases, the biological material should only be used after an independent evaluation (see Guideline 5).

Guideline 19: Transfer of a biobank

The transfer of an entire biobank for other reasons than covered by Guideline 17 should be permissible provided that the recipient’s standards of research volunteer’s protection and quality assurance are equivalent to those of the original institution in charge of the biobank. Implementation of security to ensure confidentiality of genetic information and long term conservation of genetic material should be in place before transfer is done. The transfer of a biobank without research volunteer consent is acceptable only if the samples and data have first been unlinked anonymized and ethical approval was obtained.
Definitions

Anonymous, unidentified
Biological materials that had been originally collected without identifiers and are impossible to link with their source are anonymous, unidentified. This status of confidentiality is very unusual in nutrigenomics research and therefore was not included in the guidelines.

Anonymized, unlinked
Biological materials that were originally identified, but have been irreversible stripped of all identifiers and are impossible to link to their source. (see Figure 1, see Figure 2)

Identified, coded, linked
Biological materials which, alone or in combination with associated data, allow the identification of the research volunteers concerned either directly or through a code.

- The user of the material and data have access to the code (coded)
- The user of the material and data have no access to the code which is under control of a third party (linked anonymized) (Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin, Article 3)

Relevant documents
[ 50 ] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin

Identified, nominal
Biological materials have the status identified or nominal to which identifiers, such as name, patient number, or clear pedigree location, are attached and available to the researcher.

Biobanks
Biobanks are defined as collections of samples of human bodily substances that are or can be associated with personal data and information on their donors.

Biobanks for nutrigenomics research have the following features:

- The sample collection has a population basis.
- The sample collection was established or had been converted to a sample collection in order to supply biological material for multiple research projects.
- Associated individual data exists which may include or be generated by the possibility to link to genealogical, medical and life style data bases.
• Individual data may be updated regularly.
• Biological material is received, processed and stored in an organized manner.

Relevant documents

[ 50 ] Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin
[ 3 ] Biobanks for research
Comments

Legal consequences
Participants should be made aware of possible consequences of having genotype information. It might have for them or their relatives with regard to their private lives more disadvantages than benefits. This include possible obligations to disclose this information to third parties (e.g. to employers, insurance companies).

Contact to the research volunteer
All information and communication tools such as advertisement, mailing, inquiry to registries etc. should be used to trace the research volunteer concerned. However, disproportionate expenses or if the donor have died are situations where the renewal of consent is unreasonable.

General consent
It should be possible to give a general consent for the use of the individual's samples and data for certain kinds of diseases, e.g. in atherosclerosis and cardiovascular research. However, if their use in a different type of research such as cancer research for instance or infectious diseases is intended, it should be subject to approval by an ethical committee. If the kind of research is ethically controversial, like human cloning, the research volunteer herself/himself must be asked for consent even if the legal situation allows this kind of research.

Continuous update
Continuous information to study volunteers can for instance be achieved by maintaining a special website for research volunteers, newspaper articles, or other mass media.

Protect
In order to assure privacy, data protection officers should request the utilization of all appropriate physical safeguards (e.g., locked file cabinets, locked rooms) and security measures (e.g. password access, encryption) to protect records from unauthorized access. Backup files/tapes and archived records should be subjected to the same measures. Staff training and periodic audits should be conducted to reinforce the importance of confidentiality safeguards.

Restrictions
Researchers should recognize and respect the participant’s right to place restrictions to the use on samples even if unlinked anonymized. The material could be unlinked anonymized, but still having label - e.g. "not for military research" or "not for research linked to ethnical issues".
General information to be provided to the participants
General study results on genotype effects should be communicated to the participants at the end of the study. It is recommended to invite the entire group of participants in a seminar where the study results are explained and enough room is given to ask questions.

Genotype information and individual health prediction
In general, Nutrigenomics research deals with complex diseases thought to result from the interplay between a collection of (for the most part not yet known) genetic traits and environmental and lifestyle factors, rather than with monogenic disorders caused by the mutation of a single gene. Even if all genetic traits contributing to a particular complex disease were known, genetic testing would only be able to indicate increased susceptibility, rather than the certainty of, future disease or response to dietary intervention. This is because many factors, including epistatic interactions between non-allele genes (e.g., suppression or potentiation of the effects of one gene variant by the concomitant presence of a particular variant of another gene) and present and past exposure to a collection of environmental factors, including diet and disease, might modify the phenotypic outcome of any given genotype, making it complex and difficult to interpret this kind of genotype information in terms of health benefit/risks to the individual.
Figures

Figure 1
Degrees of confidentiality of samples or data

![Diagram showing degrees of confidentiality: identified (nominal), anonymized (linked), anonymized (unlinked)]
Figure 2
Degrees of confidentiality of samples and associated data

- **Sample**
  - Identified (nominal)
  - Anonymized (linked)
  - Anonymized (unlinked)

- **Associated Data**
  - Identified (nominal)
  - Anonymized (linked)
  - Anonymized (unlinked)

The diagram illustrates the relationships between different levels of confidentiality for samples and associated data, highlighting the importance of maintaining confidentiality throughout the study process.
References


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