As part of its work on setting standards and establishing guidelines for nutrigenomics research, the European Nutrigenomics Organisation (NuGO) is developing bioethical guidelines for those engaged in human nutrigenomics studies. A NuGO working group developed a set of draft guidelines addressing four areas: (1) information and consenting prior to a nutrigenomics study; (2) the generation and use of genotype information; (3) the establishment and maintenance of biobanks; (4) the exchange of samples and data. NuGO convened a workshop with a panel of invited external experts to assess the draft guidelines. The panel of experts confirmed that these areas are important and that the development of specific bioethical guidelines for nutrigenomics research would therefore enhance the application of established international guidelines in this field of biomedical research.

Nutritional genomics: Bioethics: Guidelines: Genotyping: Biobanks

The combination of data from genome mapping projects, especially mapping of the human genome, and the availability of high-throughput tools for investigating the expression of genes has enabled researchers to begin to understand the complex interactions between nutrition and the genome that affect cell function and, ultimately, human health. This is the science of human nutritional genomics or nutrigenomics (Muller & Kersten, 2003; Fuchs et al. 2005). Although this is a young science, it is already becoming clear that food components can have profound effects on gene expression and therefore on phenotype. In addition, an individual’s genetic make-up can influence how that individual responds to specific nutritional exposures and thus explains some of the interindividual differences in nutritional needs (Department of Health, 1991).

Because of its potential to alter the way in which nutrition research is undertaken, a case has recently been made for international alliances to harness nutrigenomics for public and personal health (Kaput et al. 2005). In addition, there is a need to set standards for nutrigenomics research that will encourage the highest quality endeavour and ensure that the outcomes of such research are robust. An example of such standards is the development of databases for the systematic collection and archiving of data from microarray studies (Saito et al. 2005). Such data repositories will need to be compliant with the Minimum Information About a Microarray guidelines (Brazma et al. 2001) or other internationally agreed guidelines, and have the capacity to capture key nutritional metadata. This report will focus on the establishment of internationally agreed guidelines for bioethics in the context of research using human volunteers or samples or data from such volunteers.

Although many of the ethical issues associated with such studies are no different from those encountered in conventional nutrition research involving human volunteers, the power of the new studies to illuminate diet–gene interactions, the need to undertake the genotypic characterisation of volunteers, the new uses for materials (and associated metadata) stored in biobanks, and the opportunities for faster progress through sharing biological materials and data between laboratories (Mathers, 2004) have created a need for guidance for nutrigenomics researchers. This is especially the case where the new science has attracted researchers with limited experience of studies involving human volunteers or biological materials.
Towards bioethical guidelines for human nutrigenomics research

NuGO was established in 2004 to integrate and facilitate nutrigenomics research across Europe. The remit for NuGO Working Package 6 is to develop guidelines and standards for nutrigenomics studies in humans and models. Recognising the importance of ethical issues in this emerging area of science, one has to realise the lack of appropriate bioethical guidelines. Working Package 6 set the development of such guidelines as one of its primary objectives. To address the perceived needs of researchers in the field, this exercise focused on four specific areas: (1) information and consenting prior to a nutrigenomics study; (2) the generation and use of genotype information; (3) the establishment and maintenance of biobanks; and (4) the exchange of samples and data. A thorough search of the available biomedical, bioethical and legal literature was undertaken to identify publications with information relevant to one or more of the four specific areas of interest. In addition, an online questionnaire was developed requesting all NuGO scientists involved in human research to share their personal experiences and opinions regarding the four bioethical issues, including the policies of local bioethics committees and other regulatory bodies. In addition, NuGO scientists were asked to submit information on legal frameworks currently in effect in their country of residence.

The collected literature and input from the scientists who responded to the questionnaire were analysed, and all data pertinent to the planned bioethics guidelines were extracted. This formed the basis for the first draft of the guidelines, which was presented for critical review to a panel of independent, external experts invited to participate in the Bioethics Workshop sponsored by NuGO and held in Potsdam, Germany on 19–20 May 2005. The experts 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) and Henriette Roscam Abbing (University Utrecht, The Netherlands) represented a broad spectrum of expertise, including bioethical, biomedical, legal, philosophical and regulatory aspects of genotypic and nutritional research.

Within Europe, the legal framework of bioethics for research is given by conventions, protocols and recommendations released by the Council of Europe and the associated Steering Committee on Bioethics (Council of Europe, 1950, 1997, 1998, 2003, 2005a). Those conventions and amended protocols take on a legal character when adopted by the member states of the Council of Europe. Three finalised texts of the Council of Europe (Council of Europe, 1998, 1997, 2005a) and two draft documents addressing the use of biological material of human origin in research (Council of Europe, 2005b) and the aspect of genetic testing (Council of Europe (presumably available in 2006, personal communication), respectively, are currently available. The Convention (Council of Europe, 1997) is the general framework document defining general, most important and relatively constant principles, while additional protocols to the Convention (Council of Europe, 1998, 2005a) regulate more specific issues that reflect recent developments in the fields of biology and medicine. Furthermore, the process of re-examination of the Convention has been already started within the Council of Europe, the aim being to ‘monitor scientific developments’ (Council of Europe, 1997).

The need for ethical guidelines for those undertaking nutrigenomics research

The first issue discussed during the workshop was the need to create specific ethical guidelines for nutrigenomics research. Members of the workshop agreed that most of the international guidelines, recommendations and legislation regarding genetic information focus on monogenic disorders resulting from inherited mutations in highly penetrant genes. The genetic information acquired during nutrigenomics research differs from this in various aspects. Nutrigenomics research rarely deals with genetic information that would unequivocally determine an individual’s health status. In most cases, the genotypic information generated within nutrigenomics research projects represents influences that are often no greater than those of lifestyle factors such as diet. In addition, nutrigenomics research generates and uses genetic information whose relevance for health outcomes is not yet clear. Therefore, it is important not to put undue emphasis on the genetics aspects of nutrigenomics research and, where appropriate, to use established bioethics guidelines for biomedical research in general.

Summary of the workshop discussions

Information and consenting

The following principles were proposed. All reasonable measures should be taken to minimise the risk to, and burden on, the research participants. Studies on man that include the collection of samples and genetic data should be carried out only after the person has given free and informed consent that has been based on an adequate process of information. Special procedures should be in place to protect persons who are not able to consent (such as children and those with mental disabilities). Each participant in a study has the right to withdraw consent at any time without any disadvantages in terms of health care. Information and consent must be documented.

Genotype information

Nutrigenomics research frequently involves the determination of genotype, and researchers should guard against discrimination against or the stigmatisation of persons or ethnic groups based on genetic heritage. At this early stage in its development, genotypic information generated during nutrigenomics research is unlikely to provide diagnostic or prognostic information that will be of immediate benefit for the individual study participant. There is a danger that such genotypic information could be misunderstood or misused by the participant, his or her relatives, employers or insurers and thus
become a potential source of stigmatisation or other forms of inequity. Notwithstanding the right to respect private life (Council of Europe, 1997), which implies the right to receive any information collected on one person’s health, in the context of the current limited understanding of relationships between genotype, diet and disease risk and the very limited evidence base on what interventions, lifestyle or otherwise, may confer benefits, there is a case for consenting individuals on the basis that any genotypic information generated by the study will be kept confidential and not released to the volunteer or to any third party. In particular, wishes of individuals not to be informed about their genotype should be respected.

**Biobanks**

Biobanks are both a product of nutrigenomics research and a prerequisite for some types of nutrigenomics research. As the discipline develops, it is likely that the establishment and use of biobanks will acquire more transnational dimensions. In the field of biobanking, the most thorough, comprehensive document is the Opinion on Biobanks in Research, published in 2004 by the National Ethics Council of the Federal Republic Germany (German National Ethics Council, 2004), which gives the following definition:

Biobanks are collections of samples of human bodily substances (e.g. cells, tissue, blood, or DNA as the physical medium of genotypic information) that are or can be associated with personal data and information on their donors. Biobanks have a twofold character, as collections of both samples and data. (German National Ethics Council, 2004, p. 9)

Furthermore, the German National Ethics Council and the French Comité Consultatif National d’éthique have formulated a joint declaration supplementing their opinions on biobanks (German National Ethics Council, 2004).

In respect of the establishment and use of biobanks, two main ethical principles have to be balanced: the freedom of research and the respect for human dignity and self-determination. The freedom of research is necessary for the progress of knowledge. Progress in the field of nutrigenomics, which is aimed at the enhancement of human health through diet, will progress much more rapidly by using biological material from a large number of human subjects. The collection, storage and use of human bodily substances must be subject to the donor’s consent, which is based on voluntary agreement and information. Such consent should be couched in terms that anticipate the future uses of the banked material and data so that informed consent can be given which will allow the maximum benefit to be derived from the biobank. In most cases, it is expected that the information in the biobank will be anonymised and will prevent any links to the donor of the sample. Quality assurance measures should be in place for the generation and operation of the biobank.

**Exchange of samples and data**

To maximise the scientific potential of biobanks, access should be granted to as many research workers as possible. The implementation of this principle may, however, lead to difficulties, not least in respect of ownership and exploitation of the resulting data. In practice, research workers who have contributed preliminary work of their own to the establishment of a biobank may be accorded priority of use for a certain period. Decisions about access by others may need to be decided on a case-by-case basis. Any secondary use of data and samples from a biobank or repository of biological material by third parties must be subject to research agreements or agreements on interinstitutional material and data transfer.

**Further developments**

The Bioethics Guidelines developed through this exercise will be published and made available through the NuGO website (http://www.nugo.org) as an online tool that will incorporate examples, templates, for example for informed consent, and links to original regulatory and other documents available on the Internet. In due course, the utility of the draft guidelines will be assessed by a questionnaire circulated to users and other interested parties, and the draft will be amended in the light of outcomes of this review. The use of the guidelines will be promoted not only among nutrigenomics researchers, but also to other stakeholders, including ethical committees, scientific journals and research funding agencies. It is hoped that these bioethics guidelines will be useful as an ‘industry norm’ that will help to promote the highest ethical standards in the rapidly developing science of human nutrigenomics.

**Acknowledgements**

The authors are members of NuGO, which supported the Bioethics Workshop in Potsdam, Germany. ‘The European Nutrigenomics Organisation: linking genomics, nutrition and health research’ (NuGO; CT-2004-505944) is a Network of Excellence funded by the European Commission’s Research Directorate General under Priority Thematic Area 5, Food Quality and Safety Priority, of the Sixth Framework Programme for Research and Technological Development. Further information about NuGO and its activities can be found at http://www.nugo.org. We thank the invited panel of experts for their contribution and Herbert Piechot for the generation of the online questionnaire and his technical support of the workshop.

**References**


Council of Europe Steering Committee on Bioethics (2005a) Additional Protocol to the Convention on Human Rights and Biomedicine,


