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From: Debra_Harry@together.org
Reply-To: Debra_Harry@together.org
To: jarnstrg@web.apc.org, socioamb@ax.apc.org, ien@igc.apc.org,
iitc@igc.apc.org, saic@igc.apc.org, kdawkins@igc.apc.org,
beb@igc.apc.org, mteitel@igc.apc.org, tonatierra@igc.apc.org,
rafiusa@igc.apc.org, rafican@web.apc.org, gwatch@neu.edu,
phil@uwtc.washington.edu, cni@igc.apc.org
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Good News! At the recent International Bioethics Committee meeting at UNESCO headquarters in Paris Luigi Luca Cavelli-Sforza failed to enlist UNESCO's endorsement or support for his Human Denome Diversity Project. The critique of indigenous peoples and others has been well received and incorporated in the attached draft report on Human Populations studies. Feel free to comment on the draft. Comments should be sent to Darryl Macer at: macer@sakura.cc.tsukuba.ac.jp
He is a member of the IBC subcommittee on Human Populations.
Thanks for your input and support.
Debra Harry

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Resending

Dear Aroha, Antonio, Alejandro, Debra, Beatriz, Jean, Sandy 2 October, 1995

(Please someone send to Antonio Gonzales. I cannot send to his Email net(peace net: IITC) on my server)

It was very good to meet Antonio, Alejandro, Debra, Peter and Sandy in Paris, and the subcommittee had a chance to revise the report. The latest version is included in this message. Please send your comments to me by the 24 October, at the latest (earlier is much better). Our subcommittee members are also working on the draft, which has also been send to several population geneticists. I also posted a copy to Julian Burger of UN ESC in Geneva as Antonio suggested, and Patrick Harricknen and Mililani Trask by post.

The discussion at the meeting was short but covered a range of opinions and generated much interest. You may note in the conclusion we do not endorse any specific project, and we do recommend an ethical review committee with multidisciplinary interests and reps from indigenous groups. Such a committee may include the members of our current subcommittee plus reps from WHO, CIOMS, HUGO, as well. About a moratorium on the HGDP, it is not

considered possible, however we do suggest sanctions for researchers of any project who conducts genetics research without individual and group consent, and this may help avoid some of the abuses of the past.

We hope that this process helps dialogue. I should inform you all that 2 weeks ago I was made one of the members of HUGO Ethics committee, previously I was not involved with HUGO. I hope this is a positive sign.

Also the person who made the first draft of the sanctions section is Bartha Knoppers of Canada, who is the other UNESCO bioethics committee on the HUGO Ethics committee.

With best wishes,

Darryl Macer

<http://www.biol.tsukuba.ac.jp/~macer/index.html>

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UNESCO IBC Population genetics subcommittee draft report - 1 Oct 1995 1

Bioethics and human population genetics research

Penultimate draft report of UNESCO International Bioethics Committee Third Session, 1995, from the subcommittee on bioethics and population genetics. Draft of 1st October - still in a process of review among the subcommittee members, but this early draft is provided to ensure full comments can be given before the last deadline below. Please send all comments to Dr Darryl Macer, Institute of Biological Sciences, University of Tsukuba 305, Japan (Fax Int+81-298-53-6614; Email: macer@sakura.cc.tsukuba.ac.jp) by 23 October, 1995.

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1. Population genetics

1.1. What is population genetics?

Population genetics is a discipline studying individual genetic variation, including relevant aspects of population structure, social and geographic variability of DNA sequences and their frequencies. Their changes in time and space are controlled by evolutionary factors, among which population geneticists recognise as most important: mutation, natural selection (i.e. differential mortality and fertility of genetic types), drift (stochastic fluctuation tied to the demographic size of populations) and migration.

Population genetics deals with the characteristics of genes within a population as opposed to the description of the genes in a particular individual.

The relationships of human population groups can be studied, and the theory of evolution, questions of broad interest to the understanding of human history. Population studies are not new, and in fact large surveys have been conducted all over the world in the last seventy years. Classical studies of genetic diversity have been dealing with antigen, protein and enzyme polymorphisms, for example HLA or blood groups. Modern genetic studies are based on the molecular analysis of DNA polymorphism. Classical studies look at expressed sequences, which represent less than 10% of the genome, whereas molecular genome diversity studies are mainly concentrated in parts of the genome that are often not expressed at the phenotypic level.

1.2. Main trends in population genetics research

1.2.1. Genetic epidemiology

Isolated populations are the main source for observation of genetic forces acting in human evolution. Gene frequency across different populations does vary for specific diseases; however the total effect of genes on mortality appears similar. Pedigree information can be used to observe migration, to measure the mean-inbreeding coefficients, or to trace the linkage of disease. The method used to make a pedigree sheet, and the information sought, depends upon the objects of investigation, the quality and quantity of basic data, and their purposes. In some studies, additional clinical investigations on the hereditary diseases, or common diseases of polygenic inheritance, are included. These epidemiological surveys have been conducted at the ethnic, regional or transnational level, according to the disease studied (e.g. Tay-Sachs disease in Aschkenavic Jews, cystic fibrosis in Europe, North America and recently other countries).

Comparative studies can be made on the differences in the mortality and fertility as well as on anthropometric data between consanguineous and non-consanguineous groups. They can be used to test genetic susceptibility using polymorphic markers in different communities, which can also examine genetic susceptibility to environmental agents, and this makes possible the prevention of certain multifactorial diseases by careful avoidance of exposure to environmental agents.

Consanguinity and large family size are very interesting for population genetic studies, but studies of consanguineous marriages of families have the potential to raise numerous ethical and social issues. There are opportunities for genetic epidemiological research in countries where consanguineous marriage is a long-standing tradition. Such research projects can use data from many sources, for example, birth and death records, family register books, or anthropological or medical surveys, and socio-economic data in order to test inbreeding effects.

1.2.2. Genetic screening

Population genetic studies are not new. What has evolved very quickly is the technology and level of analysis. The first genetic studies in populations came from surveys all over the world looking at frequencies of single gene diseases. This was followed by the laboratory analysis of blood samples for the establishment of allele frequencies; blood groups, HLA proteins and enzymes all over the world. Some of these studies were done on banked blood samples that were anonymous in character. Others were conducted however, on sampled individuals from target populations, some large and open like for instance on Europeans, or others small and isolated, like those on Basques - linguistically, culturally, religiously or geographically isolated.

Based on these studies, mass screening programs for particular disease genes were adopted as was the case in Cyprus for thalassemia, or in many countries for PKU in newborns. Genetic screening and genetic testing have been discussed in another report of the UNESCO International Bioethics Committee, and by numerous other persons and organisations over the last twenty years (some refs). Many of the issues in current genetic screening programmes are relevant to population genetic research, but many are different. Moreover, while at the present we are focusing on research we should also foresee the applications and benefits flowing from the human genome project that could well apply to whole populations. Therefore the ethical considerations must be carefully treated, since whole groups of asymptomatic individuals are the targets rather than single individuals who come forward themselves.

1.2.3. Spatial and temporal variation

More recently, molecular biology has enabled geneticists to work out the spatial and temporal variation of gene frequencies. Several projects have started independently in different countries as well as an international addition to the human genome project (HGP), the human genome population diversity project (HGDP). Some studies look basically at molecular variation among populations, whereas others analyse genetic diversity in the broader cultural context. Samples could be and often are analysed from all over the world, but often for genetic studies the more isolated homogeneous human groups are thought to be the most informative. Some of these studies focus also on ancient DNA, since links between present day human groups are presumably to be confirmed through ancestors of those human groups alive today.

1.2.3.1. Multidisciplinary approaches

Genetic diversity is increasingly being seen in a much broader context. In some cases, local geneticists have been interested in the study of human diversity of the indigenous inhabitants of their countries, understanding from the beginning that only an interdisciplinary, holistic approach to this issue is capable of providing a reasonable view along with a reevaluation of cultural and genetic diversity of populations. In this report the word indigenous is used in a broad sense to mean a person that lives in a given part of the world, but not only meaning the original inhabitants (cf. UN Economic and Social Council, Commission on Human Rights, reports on Indigenous Peoples). Research projects covering most

disciplines, including anthropology, architecture, arts, bacteriology, dentistry, design, musicology, nursing, nutrition, philosophy, and medicine, as well as health care services, provide joint efforts to perceive all the peculiarities of isolated communities and give a much more broader picture of the cultural and biological responses to environmental conditions, as well as of their understanding of health and disease, natural laws that guide agriculture, settlement and architecture, etc. as well as of their cosmogonies.

There is a trend to involve broad multidisciplinary approaches in sampling of populations and this allows for the participating of the community in the research. An example is the "Expedicion Humana" in Columbia in 1991, where the Human Genetics Institute from Javeriana University in Bogota invited the whole University to join them (as described in the background report by G. Keyeux). A total of over 60 research projects, and a big health care service group was also created. The aim of the "Expedicion Humana" is to study the human diversity of a region of America which has been an important point in its populating and in migrations from Asia to America. Teams of 25 to 30 people from all the disciplines travelled to the communities. In each community that had previously been contacted and asked for consent, the investigators explained the different aspects they were interested in.. The community was asked to participate and consent once again. The physicians, nurses, bacteriologists and dentists treated more than 10,000 people for their illnesses (in a population where 2,000 samples were taken). The information collected through all means (questionnaires, drawings, records, etc.) is still being analysed and some has already been published in a series of books

This approach to the study of the diversity of populations is less reductionist than just looking at their genes, and we would recommend such more humanistic ways of understanding the role of science and scientists. It creates, however, the expectation of follow up and continued intensive interest - essentially a complete medical service - which may be difficult to maintain unless special structures were created, which would be expensive. This is usually outside the power of individual researchers or research groups, and requires strong external financial interventions, most probably by governments.

1.2.3.2. Human Genome Population Diversity Project

One example of population genetics research is the Human Genome Population Diversity Project (HGDP) is described by L. Cavalli-Sforza as "an international anthropology project that seeks to study the genetic richness of the entire human species" (Cavalli-Sforza, 1994). The name comes from a proposal in 1991 in the Journal Genomics to make a systematic study of the genetic diversity of human populations. However, like the Human Genome Project, it shares a much older origin in the work of population geneticists for many decades (Macer, 1991; Cavalli-Sforza et al., 1994). The Human Genome Organisation (HUGO) responded to the 1991 proposal in the Journal Genomics by establishing an ad hoc committee to develop the global project, and in January 1994 the Council of HUGO approved HUGO's continuing oversight of the development of the HGDP (HGD Committee of HUGO, 1994; Kahn, 1994). The HGDP is being developed under the auspices of HUGO to promote global involvement and coordination.

The scientific aims of the HGDP stated in the 1994 HUGO Summary Document are:

- a) "to investigate the variation occurring in the human genome by studying samples collected from populations that are representative of all of the world's peoples."
- b) "and ultimately, to create a resource for the benefit of all humanity and for the scientific community world-wide. The resource will exist as a collection of biological samples that represents the genetic variation in human populations world-wide and also as an open, long-term, genetic and statistical database on variation in the human species that will accumulate as the biological samples are studied by scientists from around the world."

The main scientific value of the HGDP is stated to be:

- a) deepening our understanding of human history and identity.
- b) gaining knowledge about the environmental and genetic factors involved in predisposition and resistance to disease, so-called genetic epidemiology.
- c) encourage the development of local laboratories where the collection of genetic samples will be collected and analysed.

Even though to date there have been numerous studies on the development of culture, language and population genetics, (e.g. Cavalli-Sforza et al., 1988; 1992; Sokal et al., 1992; Feldman & Zhivotovsky, 1992), and some consistency between genetic, cultural and linguistic observations has been found, a survey of more populations in a more systematic way will extend what we already know and test current theories.

Linguistic differences suggest there are about 5,000 population groups in the world. In the near term the HGDP will attempt to study about 500 of these populations, but if some populations refuse to enter the project, there are other populations that could be surveyed, so the project can be expected to obtain samples from a large number of willing populations. If funding does not permit such wide sampling there is still scientific merit in collecting data from a smaller number of populations (e.g. Cavalli-Sforza, 1995).

The HGDP initially planned to centralise the collection of samples from isolated populations, some of which are already under investigation in population genetics research. This led to fears among some members of indigenous groups that the knowledge could be used for further ostracisation (Lock, 1994). However, the HGDP is now moving away from both the idea of central control to regional control and from the focus on indigenous populations, to include all populations. Personal anonymity would be maintained by not having the names of individuals in the central repository, and by observance of established privacy rules.

The establishment of cell lines allows maintenance of a permanent record of the DNA of individuals of a population. At least two independent and physically separate collections in different countries should be kept, to maintain the resource. The HUGO HGDP committee has said that access will be free, with some compensation for maintenance costs. Any data would be shared back into the main database, which would also include computer

databases of genetic map and sequence data. There are also efforts to develop less expensive storage and microsatellite marker techniques that can be used in local laboratories that have limited resources, to ensure their fuller participation.

1.2.3.3. Analysis of ancient DNA

One of the recent trends in genetic studies is the analysis of ancient DNA samples, from fossils, preserved body remains, hair, or basically any body remains that contain DNA. There are scientific doubts about how much mutation occurs over the course of time of storage of the remains, however, these materials are providing an extra source of material for evolutionary studies.

For example, the 7,000 year old frozen corpse found in the Austrian Alps has been used for analysis (Bahn & Everett, 1993), but it may be impossible to find the appropriate persons to give consent. The question is also related to the use of tissues from those who are recently deceased. In 1995 a urologist extracted sperm from a corpse in the New York city morgue at the request of the deceased man's widow. The sperm are in cryopreservation awaiting the widows entry to a local IVF clinic ("Sperm extracted from corpse in world first" Guardian (21 January 1995), 12). Specific cultures may have very strong objections to these practices. DNA samples can be taken from the recently deceased and even sacred but archaeologically interesting sites such as tombs or battlefields. There could be no doubt that such samples would provide all sorts of interesting historical insights about the continuity of racial settlements and migration. Should however the anthropological interests outweigh the cultural and religious values about respect for the dead?

The ownership of these samples is sometimes claimed from those who believe the persons were their ancestors. In Israel there is a law requiring immediate reburial of all ancient body remains no matter which religious group they are thought to come from (Science ref to add). In Australia there are laws to require return of tribal ancestors for tribal disposal rites. In both these cases scientists have been prevented from physical anthropology studies by such laws. This raises a special kind of group consent concern as discussed later. Peoples of most countries who have lost persons in war or disasters also call for the return of human remains. Can samples be taken?

2. Ethical issues of population genetics research

2.1. Philosophical basis

The ethics of population genetics should be formulated with reference to the minimal agreed human values as expressed in international human rights law. These agreed human values are based upon recognition of the inherent dignity and of the equal and unalienable rights of all members of the human family. The rights of particular cultural groups to selfdetermination, including the safeguarding of cultural norms which are not in conflict with fundamental human rights, are then to be respected by research scientists. The Universal Declaration of Human Rights and the various treaties codifying human rights that have been developed from it are now all part of international law (Harris 1991). Not only are all nations bound by human

rights obligations in international law, so also are (1) international organisations, (2) certain special entities such as the Vatican, (3) special individuals such as diplomats, aliens, refugees, slaves, minorities, and (4) persons, corporations and governments. Individuals are bound by the ius gentium in so far as human rights are at issue (Green 1987).

Central to our human rights obligations is the promotion of "respect for, and observance of, human rights and fundamental freedom for all without distinction as to race, sex, language, or religion." (Charter of the United Nations, Article 55 (c)). The Universal Declaration of Human Rights is founded upon the notion that there are universally recognised human values and that these values are inherent in the human individual. In the Preamble the Declaration states that "the foundation of freedom, justice and peace in the world" is the "recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family." (Fleming 1995).

The equality with which "all members of the human family" are to be treated as far as human rights are concerned precludes all attempts to exclude from moral consideration human beings deemed to be nonpersons. There is no philosophical agreement in the international community as to what constitutes personhood. Accordingly Article 6 of the Universal Declaration on Human Rights (1948) and Article 16 of the International Covenant on Civil and Political Rights (1966) require that every member of the human family be treated as a person, that "everyone has the right to recognition everywhere as a person before the law."

These fundamental human values expressed as human rights are an essential element to civilised society and stand against the eugenic temptation to reduce the value of a human individual to the sum total of its genes.

Human individuals have an "inherent dignity". The human rights documents do not give a reason why human beings are to be seen as having unique value. They simply bear witness to the fact that the international community agrees that each human individual is to be counted as valuable as any other human individual.. Jacques Maritaine (1954), for example, noted the practical convergence on fundamental values despite profound disagreement on ideology. Despite all the difficulties it is possible. "as the International Declaration of the Rights of Man published by the United Nations in 1948 showed very clearly ... to establish a common formulation of such practical conclusions." When one asks the question as to why these rights or values ought to be accepted there is some debate, between religious and philosophical foundations for human rights. There are also some political disputes over how human rights are to be interpreted within the framework of international law.

The ethics should also be in accordance with the ethical norms current in the culture where the research is being conducted, recognising that the degree of importance accorded to communitarian values, varies between and within countries, populations and groups. This latter point is well acknowledged by the recognition that "Minimum ethical principles must be formulated, recognizing that, in the process of collecting, the human rights of people in participating populations should be respected and that these people are partners in work rather than merely subjects of it. Any

particular region may have broader ethical concerns than those addressed here, which should only be considered as a minimum." (HGDP, 1994).

2.2. Research approach and methodology

2.2.1. Informed consent

The importance of obtaining consent from a study population is well recognised (even if not always practiced). Population genetics studies should be conducted by personnel with the appropriate qualifications, but only after informed consent has been given for any general medical examinations, and removal of blood samples (generally under 20ml) or other bodily samples. Such samples are taken to the home laboratory or other laboratories, and the components are separated for analysis. The analysis of the samples also requires specific consent that should be given before the sampling (cf. Baird, 1995).

The doctrine of informed consent is applied to both medical treatment, and research, and before a person is asked to consent to any sampling or treatment they must be provided with certain information. This information includes at least the following, which must of course, be presented in language the patient can understand:

- a) A description of the procedure which is generally easy, and should be risk free if accepted medical procedures are used for sampling.
- b) A description of the risks and benefits of the resultant information.

It is worth noting that the need for consent to be "informed" may be objectively impossible to be achieved. Even when correct information is carefully presented in culturally appropriate ways, it cannot be guaranteed that it has been understood. The ethical obligations that are achievable include the accurate delivery of information together with the disclosure of relevant risks and benefits to the individuals and communities involved, and having regard to the legitimate cultural and religious needs and aspirations of particular communities, especially in the way in which consent is ultimately given. We should not speak so much, then, of "informed" consent as of an obligation or duty on the part of scientists to inform participants of the relevant information.

The application of the ethical principle of informed consent and respect for integrity is a more complex process at the level of populations. In order to ensure that the understanding of the goals of research, of the risks involved, of the use of research results, and of the rights of the groups and individuals under study, careful consideration is needed. The lines between genetic testing of individuals, genetic screening within one's own population, and population genetics research of other populations and groups, are not always clear. It is clear that we do not ethically require group consent for most genetic testing, though society may draw lines even at the freedom of choice of genetic probes for nontherapeutic purposes (e.g. sex selection is banned in several countries). The fact that some recent population genetic studies may involve investigation of several hundred genes between single individual representatives of different populations makes the question of group consent extremely difficult.

There are various levels at which consent may need to be obtained for

studies of population groups. High level governmental approval is in many countries mandatory for studies on specific populations of persons. Such official clearances need in every instance to be complimented by consent from the individuals and the local groups/communities selected for study whether the consent is obtained directly or through formal/informal leadership, group representatives, or trusted intermediaries.

It is important to identify both the most appropriate persons with whom to communicate and from whom to obtain clearance, and also what are the appropriate content and media of communication. Research will need to take account of the group, social organisation, goals and aspirations, cultural values and mores, and laws (both statutory and customary). If the research methods involve the use of saliva, skin, hair, or blood samples, etc., it is necessary to ensure that the collection of these body samples does not violate cultural norms and concepts relating to the human body and its functions. The ways of approaching the communities must always take account of the particular social and cultural organization and laws. Sometimes the leader or the individual chief of a family or familial group is the person who gives consent for the other members of the community to participate in the enquiries and biological sampling. These persons may be difficult to identify. Of course the most difficult group consent question is who can give group consent for the genome project itself a question that no one has been able to answer (Macer, 1991).

Various groups of indigenous peoples have expressed their irritation with past population genetics research which they claim has been conducted without prior consultation and in a way where consent was obtained in terms consistent with their cultural norms. Practitioners of contemporary science do not always understand that the goals and aspirations of scientific projects may not always coincide with the goals and aspirations of particular cultures. It may not be ethically acceptable to some people to cooperate in the collection of saliva, skin, hair and blood samples for the purpose of storage and the establishment of "transformed cell lines", samples which would be basically identical to the individual of origin which are then made available for study to scientists around the world. Therefore many representatives of indigenous peoples have expressed strong concerns about the HGDP. An important outcome of this concern and the HGDP project may be the more active participation of some individuals of the community in the research projects, as well as in the better formulation of precise questions that researchers try to answer through their observation or laboratory work. These concerns apply to sampling within any population genetics project.

In order to bridge gaps between scientific goals and aspirations on the one hand, and cultural goals and aspirations on the other, it will be necessary for scientific information to be communicated to individuals and communities in terms that can be understood by those communities, and if they exist, by individuals acceptable to, and counted as trustworthy by, those communities.

It will not only be necessary to identify the correct person or persons to give scientific information, but also to identify to whom the information should first be given, and what cultural mechanisms apply to the giving of consent. This will involve taking account of the fact that individualised notions of obtaining consent which tend to dominate in liberal

Western societies cannot be applied carte blanche to people of other cultures. In secular liberal societies consent is seen as an "informed" expression of an individual's selfwill and autonomy. Consent is deemed to be informed if the subject is exposed to all relevant information, including risks. Other cultures of course may place greater emphasis on the advice of leaders who represent the continuity with traditional wisdom, or with the fate of family or group members. Relevant factors for moral decisionmaking in communitarian societies may derive from sources not as empirically accessible as medical data.

The moral and spiritual values which have profoundly shaped the cultures of different population groups may well result in deeply held convictions regarding bodily and familial integrity (Paulette, 1993). Information about genetic inheritance is loaded with emotional, historical, cultural, and religious significance, which may differ in different cultures and religions. The form in which the consent is given needs to be culturally appropriate as well. Not all communities are governed by bureaucratic paper consent forms and written signatures. The form in which consent is given will need to be discussed and agreed upon by each community.

2.2.2 Selection and participation

The participation of the study group in various stages of research is one good way of keeping open communication and of developing trust between researchers and research subjects. Such anticipation may take various forms depending on the situation. In international research projects, the involvement of the local scientists, if possible, and consultation with local groups, is an effective way of ensuring that communities or indigenous populations are treated with sensitivity, respect, and wisdom.

Long standing prejudices about racial differences may colour and direct the selection of subjects for investigation and the sorts of interpretations made. Sitting targets for investigation need not be restricted to racial groups. For example, biomedical experiments were performed on more than 23,000 persons in about 1400 different US Defence Department projects for over 30 years after the Second World War. The selection of target populations was clearly made on groups who were judged to be sitting targets, such as "soldiers, prisoners, those considered to be mentally defective (both children and adults), hospital patients with terminal illnesses, and pregnant women if the women were poor." In these experiments subjects were exposed, often without their knowledge, to radioactive contamination, nerve gas, LSD and various biological agents. "Permission or informed consent to carry out these experiments was generally not sought at all or not given." (Estling, 1995).

Because the HGDP was planning to collect blood samples some groups called the HGDP the "Vampire project" (Lock, 1994), and some groups were angry because they believed that they were possible target populations even though no community representatives had been contacted about the Project. The Mataatua Declaration on Cultural and Intellectual Property Rights of Indigenous Peoples of June 1993 is a call for a halt of the HGDP until its impact has been discussed. Article 3.5. of the Declaration calls "for an immediate halt to the ongoing 'Human Genome Diversity Project' (HUGO) until its moral, ethical, socioeconomic, physical and political implications have been thoroughly discussed, understood and approved by

indigenous peoples". The Declaration is actually not antiscience, and includes a call for involvement in scientific research, recommendation

2.11. "Ensure current scientific environmental research is strengthened by increasing the knowledge of indigenous communities and of customary environmental knowledge". Since that time, the HGDP goals have shifted somewhat, but there has been a series of Declarations directed against this project (Mead, 1995). The HGDP Summary Document includes ethical guidelines which do address the question of participation, consent, and commercialisation. Nevertheless, the controversy continues and as recently as February, 1995, a forum of Indigenous Peoples in Asia issued a statement to the European Parliament in which they strongly opposed the HGDP and called for it to be stopped (ARCW, 1995). However, on 18 July, 1995, the UK House of Commons declared its supports for the project (Ref to check!!).

Therefore we would urge researchers to consider the history of the group that they plan to include in their research, regarding not only the scientific interest, but to think of ethical, social and ideological factors that may come back to that group after the research. The funding mechanism for the Human Genome Project in the European Community was delayed until a system for funding ethical, legal and social impact (ELSI) issues was established. In Canada up to 13% of the Human Genome Project has been spent on ELSI and educational issues, and in the USA 35% is allocated. The ELSI issues do not only relate to genome research, but to all of genetics, and science.

2.3. Utilisation of research results

2.3.1. Confidentiality and access to information, management of genetic databanks

As has already been well documented from the practice of genetic screening the personal impact of genetic information is significant. DNA collected among groups would present analogous problems relating to the adequate protection of privacy whose meaning and value might vary across cultures.

Issues related to individual privacy and possible abuse of genetic data (by insurance companies, employers) are considered in the UNESCO IBC genetic screening report of 1994. Nevertheless, it is important to note that in population genetics research, confidentiality issues have to be discussed at the community level as well as at the individual level. One way of ensuring confidentiality for individuals would be not to collect or keep identifying information in the central repository. We recommend that confidentiality for all individuals, and in all human population genetic research be protected in particular through coding and anonymity, unless the individual wants to know.

An interesting point is that while personal anonymity should be able to be maintained by not having the names of individuals in the central repository, in certain cases would there be provision for classification of sensitive information about one population group from general databanks? Where does the privacy claim stop, at the individual, family, village or population? Another issue could be if all members of a population have a common late onset disease, afflicting them at age 40 years. Would that information be general knowledge or protected? Health insurance companies could cancel or refuse health insurance to a population, in the same way as

they have done it for a single individual or family with these kind of presupposition. In several countries these family cases have led to legislation on genetic privacy, and although the principle is included in the UNESCO Declaration on the Protection of the Human Genome further national efforts at protection of privacy may be required.

Population genetics extends the ethical issues of large pedigree genetic research. Population genetics research can benefit from the lessons learned in the studies of large family groups. One such lesson is about preserving confidentiality (Annas, 1993). There are also general lessons to be learnt from other genetic testing programs, and human genome research however, if none of the personal data is shared with the members involved in the project than there are fewer dilemmas. We do recognise that there may be cases where useful information for a person may be found, and there is some ethical argument to support disclosure to that individual however, those cases may be exceptions to the general purpose of population genetics surveys.

Although information regarding the identities of community samples may be restricted, in all probability, anyone who really wanted to identify communities may be able to do so. Moreover, access to such information may be relevant to insurance companies, who then may be reluctant provide medical insurance to a community, or even a population group, known to have a gene that predisposes them to a particular disease, for example. This is similar to the case where health insurance may be denied to a single individual or members of a family in countries that do not prohibit genetic discrimination by law. Thus, national legislation will have to be enacted to protect against such abuses. Genetic information about a particular minority could be exploited by states for political purposes such as repression. The difficulties involved in guaranteeing the maintenance of absolute confidentiality should be discussed in the process of obtaining informed consent. Further, the keeping of genetic material in central repositories may be ethically and politically sensitive.

2.3.2. Patents, commercial rights to celllines and DNA

Patents granted on cell lines of persons have been opposed, subsequently withdrawn, or are still pending. Patents are opposed on two levels: One is the opposition to any possible patenting of "life", which includes microbial, plant, animal and human life. This position is taken by NGOs, and indigenous populations, as well as some academic groups. The second level questions whether population groups (whose gene products may subsequently be patented), are or should receive commercial benefits. This concern arises from experience in the patenting of agriculture and pharmaceutical products which have been developed by corporations from genetic materials and knowledge collected from the third world without any benefits accruing to the original donors of the genetic material.

The question of the "ownership" of DNA, still more the notion that genetic copies which once belonged to human beings can be said to have proprietary value, has already been extensively debated regarding organ donation and the patenting of human genes. These issues have arisen in population genetics primarily in relation to the patenting of genetic material taken from indigenous peoples. In 1993, a patent filed by the United States government on the cell line of a 26 year old Guaymi Indian woman from Panama was opposed by the Guaymi General Congress, the World Council of Indigenous Peoples, the Rural Advancement Foundation

International, and the World Council of Churches (RAFI Communique, Jan/Feb 1994). The patent claim was subsequently withdrawn, but other patent claims are still pending and being opposed.

To introduce briefly this issue, one of the first declarations on gene patenting stems from the ICSU Statement on Gene Patenting in June 1992: "Information about nucleic acid sequences cannot be patented per se. Such sequences should be patentable solely within the context of their demonstrated significance and/or application and not of their potential products." Furthermore, "the process of discovery leads man to identify natural laws, mechanisms or objects (elements) which already exist independently of human beings. Invention on the other hand is the process whereby humans can construct new elements that they can use. Invention is the result of human ingenuity and knowhow. Under these circumstances, no one can have the right to monopolize a discovery, as every discovery is part of the natural order to which human beings themselves belong. The human genome cannot be patented as such. Identification of the genome, and of the genes of which it is made up and of the nucleotide sequences which describe the composition of these genes, constitute a discovery. In addition, the human body (and its component parts) cannot be regarded as an asset, it cannot be marketed and hence cannot be a source of financial gain" (Pompidou, 1994). The philosophical basis of the objection to patenting is the argument that life is recomposed, not invented.

Patents have been awarded for transgenic animals, which bear genetic engineered human genes or gene regulators in specific tissues, as models for studying the expression of human diseases or as source of useful proteins of human origin for therapeutic use (for reviews see Grunkemeyer and Cosgrove, 1993; Cosgrove et al., 1994).

One of the goals of population genetics research, such as the HGDP, is the creation of cell lines. Patents have already been granted on immortalized cell lines and hybridomas which are useful in research or as monoclonal antibody sources for research and diagnosis. In this latter case, the hybridoma invention implies a process, which falls under the definition of patent application. These cell lines are kept, reproduced and distributed by commercial companies, mainly the "American Type Culture Collection" (ATCC) in North America and the "Centre d'Etude du Polymorphisme Humain" (CEPH) in France, which do request the cost of supply for requested samples.

Some international bodies have raised objections about this activity: A database search conducted by RAFI reveals that, by November 1992, the ATCC held 1094 cell line entries. More than onethird of these are identified as being the subject of patent application" (RAFI Communique, 1993a). One could also stress that most cell lines are of Caucasian origin (French donor families) or from patients' tissues. However, these services are expensive and laborious work for any laboratory, and only companies like these can afford to maintain a large variety and number of cell lines available to all researchers. There does need to be some major cell line collections, and virtually the ethical issues that relate to population genetics research apply to other cell collections obtained from other persons.

In France in 1994 there was debate over the commercial access to a DNA and cell bank collected from 800 French families, the Centre d'Etudes du Polymorphisme Humain (CEPH). The issue was divisive, as some funders

wanted to ensure free access while there were claims that exclusive commercial access would increase support (e.g. Nature 368 (1994), 175; 368 (1994), 575). The pressure led to a deal for exclusive commercial access being dropped.

Patents are necessary in the way industrialised societies are organised as they serve to stimulate investment and technological developments that are necessary to manufacture these products and provide the services they entail. But all the actors involved in this process, whose participation leading to the final step of production is unquestionable, are not always rewarded proportionally to their input as stated by Third World concerns.

Their concerns are to do with the ever increasing gap between wealthy and poor societies.

We should also note that public opinion around most of the world is against patenting of human DNA (Macer, 1994), although we recognise the issue is complex and there needs to be some protection of commercial investment in research to encourage further development of medicines and biotechnology products. There have been discoveries and inventions which have been made without desire for patents, but most research funding is currently judged as an investment, and the trend is to become more commercial.

This trend is indeed a worrying one. By prioritising the objective of financial benefits, scientists, and in particular human molecular geneticists, are converting themselves into science merchants, who are led by the possibility of commercialising research results rather than, what had been in the past, by what many consider to be the nobler aims of discovering knowledge. If a practical application follows a novel result it has always been a highly welcomed scientific output, but the focus on patentability is a reductionist way of practicing science.

The intellectual property rights system was developed by the industrialised countries, theoretically, to reward intellectual innovation and invention by protecting inventors and guaranteeing the publication of new information. Worldwide, 95% of the patents are issued by so-called First World governments to First World corporations, while 4.8% are issued to foreign transnational companies operating in other countries, with only 0.2% issued to non-First World inventors. This may represent formal research investment, however, it neglects the much greater contribution of historical agriculture and traditional medicine in Third World countries to the world economy. This is a principal concern of Third World countries and as genetics becomes more commercial, so will the concerns grow (Gupta, 1995).

When the International Board for Plant Genetic Resources was funded in the 1970s it created a public domain resource of 125,000 plant germplasm specimens. Later, some companies obtained patents on hybrids, with generally no or little return to the traditional farmers who had collected them. The same is true of medical compounds, and we can see swapping debt with natural conservation schemes as another form of commercial exploitation. In the USA several broad patents, one for genetically engineered cotton and one for genetically engineered soybean were claimed, and while the challenges to the validity of patents limited these claims, these were considered as "colonisation" of an agricultural crop by Third World countries.

The DNA databases from population genetics research may be the product of commercial research on publically obtained cell lines. There has also been much debate over the commercialisation of human cDNA in the creation of a commercial cDNA library in the USA by Human Genome Sciences Inc. The company Human Genome Sciences, which includes The Institute for Genome Research (TIGR), Gaithersburg, has released terms of the way researchers can access the 150.000 cDNA sequences it has compiled into a database, which include 35,000 of unknown function, (Nature 371 (1994), 3636, 463; Science 266 (1994), 25). Users must sign an option agreement, and companies will have 6 months to try to make joint shares in commercial developments. The release of the cDNA sequences from TIGR to the general community is under the condition that they can take first look for 30 days before publication at papers, with an option for a 30 day extra delay. The index to this database has been published as a "Genome Directory" by the journal Nature in 1995. The publication of this "commercial" directory was criticised by some academics (Maddox, 1995), and concern about gene patenting is not limited to Third World countries.

The issue of profit from population genetics research is also discussed in the draft European Convention of Bioethics, article 11, "The human body and its parts shall not, as such, give rise to financial gain". In note 90 it is noted that this does not apply to discarded tissues, such as hair and nails, "the sale of which is not an affront to human dignity". However, DNA can be obtained from discarded tissues, which makes us note that in some cultures, for example certain North American Indians, hair has religious importance as is not regarded as discarded. The assumption that the sale of discarded tissues is not an affront to human dignity might be a valid one for Western societies, but care must be taken in regard to more traditional societies who might disagree.

The Mataatua Declaration on Cultural and Intellectual Property Rights of Indigenous Peoples of June 1993 included several recommendations to member states of the United Nations. In recommendation 2.7 "Commercialisation of any traditional plants and medicines of Indigenous Peoples, must be managed by the indigenous peoples who have inherited such knowledge". In 2.8 they called for "A moratorium on any further commercialisation of indigenous medicinal plants and human genetic materials must be declared until indigenous communities have developed appropriate protection mechanisms". In section 2.9 they called for consent, "Companies, institutions both governmental and private must not undertake experiments or commercialisation of any biogenetic resources without the consent of the appropriate indigenous peoples". The Declaration also requests "cooperative rather than competitive framework", and "increase in the involvement of indigenous communities" in "research and training as well as education", that would make them participants in the process of development of industrial goods from the human genome and beneficiaries of the commercial profit, rather than being simply suppliers of samples that eventually can lead to a significant therapeutic discovery.

One of their principal concerns is that samples will be used for profit and not return benefit to the peoples who gave them. We can see the same concerns being expressed in the Asian Regional Consultation Workshop on the Protection and Conservation of Indigenous Knowledge meetings in 1995. Commercial concerns applies to all types of biotechnological patent, and there have been examples in the past from the patenting of plants and animals. The Biological Diversity Convention exists which could be used to protect the other organisms of local peoples, and we could see the same

principles applied to the knowledge and genetic information gained from DNA sampling of local peoples.

Financial gains through patenting is a form of power. Those who have the knowledge of human genome sequences hold a monopoly over this knowledge through patents, and therefore have the monopoly of commercial gains. This form of power is a way of domination which may lead to an exacerbation of the already deep gap between wealthy and poor societies, since it gives no chance to Third World countries to develop their own scientific strategies in the field of diagnosis and therapy based on publicly available gene sequences. And what about extrapolating the human genome patent claims to gene sequences of microorganisms endemic in these countries? Would they also have to give up royalties for vaccines, designed by scientific teams from poorer countries against malaria, leishmania, chagas and other diseases, the microorganism sequences of which are protected by an industrialised countries patent?

This subcommittee recommends that patenting should be severely limited to new applications and processes which may be developed in the course of human population genetics research, and conditions should be developed to ensure free access and use by researchers everywhere. This recommendation is based upon two basic points. Patents have the effect of limiting free and open scientific exchange and payment of royalties will severely limit access of scientists from poor countries to research carried out by scientists. This will exacerbate the gap that currently exists between North and South. Secondly, the patenting of naturally occurring lifeforms is objectionable for many cultures. Genetic material is part of what constitutes life, and as such, patenting transforms this into a commodity that can be owned and traded in.

2.3.3. Return of research results and financial benefits to subjects of research

The concern that sampled individuals will just be suppliers of samples who will not benefit from eventual commercialisation is common to any research subject. The question of who is the legitimate beneficiary of commercial benefits is unclear, that is, whether it should be the national government or some sort of trust fund for the population group. Benefits returning to third world countries for example, may not necessarily benefit the indigenous populations from whom the samples were taken.

Although the core of the problem is not that indigenous peoples would likely be a particular source of patentable genes for industrialized countries, neither any other human group, the concerns about accumulated royalties is as important as the actual problem of access to medical care products in general in the Third World. An interesting point of debate on royalties is the participation of individuals in population genetic studies who have been, and will likely continue to be, the most interesting "source" of gene sequences, namely, the patients suffering from a disease, whose DNA is the source of mapping, cloning and ultimately sequencing the responsible gene. If we admit that a gene sequence can be patented, then in consequence with this principle, the true "owners" of that particular sequence may be the patients suffering from the disease, and the relatives called "carriers" of the responsible gene that have participated in the elucidation of the sequence? In the same way, if a particular sequence

conferring some type of resistance or, conversely, susceptibility, to a disease should be discovered in an indigenous community, should not these carriers also have to be considered as the "owners" of the sequences?

Therefore we recommend that the groups be given the option and mechanism to enter into contracts with the researchers and with companies who latter use cell lines or DNA. This would not be on the basis of the sale of blood or other bodily tissue but on the basis of their cooperation in a scientific program which may bring large financial rewards to the companies involved, or those secondary companies which utilise the results. Money would only flow back to those groups when profits were generated from the applications derived from that cooperative venture, for example a certain royalty, or some other mutually beneficial arrangement.

It should also be remembered that financial returns are not the only form of benefits of research results which could be returned to subjects of research. A more important aspect is the return of information and research results to the communities from which data was collected. There are research projects, for example, which plan to write their research analyses and conclusions in popular form which are accessible to the communities so that they could be helpful to them in promoting concrete responses to particular problems.

Maybe the most important and novel issue that population genetic studies have provided is the return of information and research results to the communities. The analyses and conclusions must be understandable and helpful to the communities themselves. They may also promote concrete responses to overcome particular problems. For example, in Expedition Humana, books written at the layperson's level were sent back to the local peoples, local government, and all other groups that were expected to have an interest (though not all are literate!).

The most poignant problems of many populations involved in population genetics research is public health, but this cannot be understood just as a diagnosis of symptoms and consequent medical treatment. The results of physical examinations and clinical diagnosis and options for treatment are sometimes communicated to each participant in the local languages through local health authorities and home doctors as soon as possible. This is in order to utilize the health data for the improvement of local community health, especially in the remote areas or areas with poor medical care. In indigenous communities these problems are usually an intricate result of breakdown of a traditional welladapted cultural as well as biological relationship to the environment, due to economic and political pressures from the dominant society.

Provision of health and medical care, however, should be appropriate to the social context of the community and should be ongoing. In this, the principles of primary health care as contained in the AlmaAta Declaration (WHO/UNICEF) of 1978 should serve as a good set of guidelines to follow. Thus, benefits should also flow back to the groups and communities in the form of contributions and recommendations for local health care policies and education that enable communities to better their positions. Therapeutic and diagnostic benefits should flow back to the groups and individuals concerned, contributing to the further enunciation and development of local health care policies including education. However, the offer of services to the communities should take into account the traditional medical knowledge and practices of that community. The international community calls for provision of medical and other services

to those communities in need, however this must be done with sensitivity to the local culture, and these policies, as well as the health care services which are offered, should of course be decided upon by the communities.

The feedback of results to the communities concerned should help foster a greater sense of community identity in the face of aggressive cultural imperialism by industrial superpowers. However, we also note that no undue compensation should be offered to ensure participation in sampling (Knoppers et al. 1995), which may be extremely difficult to control given the onesided power relationship in poorer areas of the world.

2.3.4. Anthropological uses of the genetic knowledge

There may be some challenging implications of the better understanding human history that the HGDP will provide. The knowledge from HGDP could also be used to educate people of indigenous groups that could help protect their interests. However, the knowledge of human group evolution and the relationships of those groups to others, may challenge the views of those who did or did not participate in the research. Some population groups have strong beliefs in mythologies or cosmogonies that are different from the dominant world cultures. These mythologies may explain group origins, and identity, and the return of data that challenges the accepted relationships to other populations and their own selfidentity, is a very delicate issue. Some of these groups may not want to know the results, and do have a right not to know, analogous to the individual right not to know one's own genetic makeup. However, it is unlikely that they can be protected from eventually learning of the knowledge indirectly.

Some potential challenges include the question as to who are the first inhabitants of regional areas, the historical relationships to current national boundaries, and who has the right of government. Indigenous peoples may be able to use the claims of prior settlement to push land claims that could damage the claims of more recent immigrants and ethnic minorities. Which inhabitants of which time period do we consider to be the legally entitled owners of land that was successively colonised? The genetic data can be used to confirm or reject the information obtained from archaeology, oral and written accounts of history. In the West Pacific for example, genetic studies show that settlement was from the West not from the Americas (Clegg, 1994).

Some say that genetics will not tell us anything within a time frame that would make valid legal claims on us under a common law or civil law approach (Greely, 1995), and we could say that we already know much of human history, and indigenous peoples claims for prior settlement may be ignored despite the clear knowledge that they were there. If ancient DNA samples are collected and markers used to trace the contemporary descendants this could be used to find the genetic descendants, but these may not be considered to be "legal heirs" to the land under most legal traditions. It may be beyond the scope of the UNESCO International Bioethics Committee to consider changing the legal system of ownership that tends to overlook European colonisation of the past few centuries, but we should note that there are recent legal rulings which support indigenous people's original titles to government lands in Australia and New Zealand.

2.3.5. Other issues arising from use of research results

The issues of discrimination, eugenics, stigmatisation and other ideological uses and abuses of genetic research on populations are discussed in the following section. One fear that has been expressed about population genetics research is that "access to an IHI's (isolate of historic interest) complete genetic makeup makes it theoretically possible to devise cheap and targeted biological weapons trained solely on that community" (RAFI Communiqui, 1993b). Given the restrictions on biological warfare that already exist in international law, and the likely toughening of these sanctions, and that it would be extremely unlikely that any scientific method could be developed to make specific genocidal weapons even if someone wanted to, this fear can be dismissed. Unfortunately, much more practical and barbaric methods of so-called "racial cleansing" are available.

Eventually the genetic data could be used for genetic therapy and intervention. Many of the ethical issues are summarised in the UNESCO IBC report on gene therapy of 1994. Although it appears unlikely, it is possible that in the future a population could agree to the general use of a genetic vector to provide a medical benefit, such as immunity to an infectious disease, or compensation for a common genetic disease among a particular genetic population. Such an issue is related to the extent that traditional vaccination programs are compulsory or voluntary, and we note that such programs are generally voluntary although public information campaigns may encourage participation.

3. Public understanding

3.1. Ideologies

Public attitudes towards population genetics are often based on social ideologies, racism and eugenics and can well lead to stigmatisation and genetic reductionism. The ideologies of racism and eugenics are human artefacts, socially and politically constructed, and may well prove impervious to scientific proofs. Indeed, such ideologies may improperly appropriate scientific findings to further advance and legitimise social and political programs. Research scientists need to be aware of their own assumptions and philosophical presuppositions as well as the assumptions and philosophical presuppositions of others, and to be prepared to work within a general framework of respect for human rights as expressed in international law. The pursuit of scientific enquiry as a means to legitimate ideologies is a temptation that should be resisted. Without paying attention to these issues, scientists themselves may sometimes find themselves involved in unfair manipulations of their intentions or results, in the name of diverse ideologies.

Scientists themselves are not immune from the usual array of assumptions, dislikes, biases and prejudices that beset the wider community. Unfortunately scientists have at various times in history believed themselves to be working in a value free domain, gathering the pure crystals of data and indeed trumping other human values and concerns in their pursuit of ever higher degrees of knowledge. The matter is best expressed by Alasdair MacIntyre (1982): "Aubrey's error was of course not only to suppose that the natural scientist is a kind of magpie; it was also

to suppose that the observer can confront a fact faceto face without any theoretical interpretation interposing itself." MacIntyre concludes that it "is now largely agreed upon by philosophers of science" that "this was an error, although a pertinacious and longlived one". But while philosophers of science may now be largely agreed that "this was an error", it is still a temptation for scientists to imagine that you can stare a fact in the face and view it just as a fact.

The agreed values promoted by the United Nations are in harmony with the world's deepest aspirations as to what it means to be human and living in solidarity with other human beings, and is in harmony also with the moral insights of the religions and philosophies which have helped shaped the various human cultures. The international community has promoted by law human values to attempt to guarantee the possibility of peace within and between nations. "The high universal principles that originate in human dignity" form part of the dogmatism of international law which overcomes the radical scepticism of cultural and moral relativism, a relativism which can in other circumstances lead to the dogmatism of totalitarianism.

3.1.1. Racism

Current population studies show that the typological classification of humans into different "races" is scientifically invalid. Nevertheless "racism" as an ideology and as an attitude is a human reality. Population geneticists point out that population genetics offers no scientific basis for the belief that certain races (however defined) are superior to other races. Indeed there is a greater diversity within populations than between populations. However, care needs to be taken in the way such an argument is formulated. Variation between individuals or groups could be associated with evaluative notions of "superiority" or "inferiority", and thus foster racism.

Population studies in the past have shown that most of the diversity within the genes studied is to be found in every race or population, and if this is true then this information could be used to combat racism. Since current population studies show that the typological classification of humans into different 'races' is scientifically invalid, we should avoid the use of the term "race". Population studies include linguistic and anthropological studies. Some such studies have been misused in the past and need to be treated with appropriate expertise and care by the investigators.

Historically, Third World people in general, indigenous people in particular, have been the objects of research by scientists from developed countries. The history of anthropology is based on the study of 'exotic' races, and anthropologists operated within the prejudices of their age. One example of this is the craniometry research that was done in the second half of the 19th century when Western scientists measured craniums and ranked races by their measurements. By their ranking, the white man is the most superior race, and the black man, the most inferior, comparable to apes (Gould, 1981). We should also note that religious discrimination has been linked with ethnic discrimination.

The World Council of Indigenous Peoples was upset by the discussion that cells should be gathered from populations at risk of disappearing

(Roberts, 1992; Pahr, 1994). At that time they thought that the HGDP was aimed exclusively at sampling from endangered populations, which it should not be (Majumder, 1995). However, the HGDP does not contribute to the demise of the population groups it studies.

With the burden of this recent history, it should be no surprise that many Third World and indigenous people view Western research with suspect. Researchers have responded to this by evolving research methods which involve their subjects in a more participatory fashion, or by developing research projects which do not only aim to study, but also to share research findings, and whatever benefits which accrue from it, with their subjects. From this, the rhetoric of making research subjects partners in research has emerged. One should question what this rhetoric means. Whose research agenda is it, for example, or whether the research addresses the concerns of the researched subjects.

Indigenous peoples' organisations now question the purpose behind research that is done on indigenous population groups. In certain parts of the world, indigenous peoples are facing cultural extinction. Where there is mass logging of tropical rain forests, for example, indigenous people who live there are depleted of food and water resources, and driven from their homes. They eventually join the ranks of waged labourers in logging camps and cash crop plantations. As their social fabric breaks up, they are in danger of losing their identity and culture. The struggle to survive as a people is a pressing concern of many groups. In this context, the call for researchers to collect genetic materials from indigenous populations before they disappear as distinctive genetic groups would appear grossly insensitive and callous. Furthermore, if such research receives funding from governments, the money and resources could be channelled from other pressing needs.

Populations have mixed in the past and mix more today, and some cultural anthropologists suggest it is difficult to define linguistic and genetic populations (Lock, 1994). In attitudes to bioethical questions we also find broad diversity across many cultures. This is seen in the International Bioethics Survey performed in 1993 in a variety of countries, where there was a similar range of diversity of ideas in numerous open response questions on issues such as images of disease, nature, life and genetic technology in each country, and the range within each country corresponded to the same range found between all (Macer, 1994). In this way we could see cultural diversity in a similar way to genetic diversity, neither supports the notion of race.

It has been amply demonstrated that, while there is a wide range of diversity between human individuals, the average differences among human groups are small. Accordingly, there is no scientific basis for believing that there are races which are more 'gifted' or 'smarter' or 'better', and thus racism is not supported by contemporary scientific research. However, this argument needs to be carefully expressed or it may unwittingly appear to rely on the assumption that if you could in fact demonstrate that some races were more 'gifted' than others, had 'better' or 'smarter' genes than others then those races would be superior, and the other races inferior.

All population genetics research should be carried out in a way that is sensitive to the ethical obligations found in international law. However, we should also be clear that those who seek to use the findings of population genetics to support movements and ideas which are hostile to fundamental human rights will no doubt do so. The correct response to this

is not to say that the findings will prove the opposite, i.e. fight against racism, but to recognise that what science finds is what science finds, and these findings should be put in support of fundamental human rights which derive from the universal belief in the inherent dignity of the human individual. Such values cannot be "proved" by science, and neither can they be "disproved" by science. UNESCO should actively encourage greater public acceptance of variation and vulnerability, and promote the value of human diversity. While there are fundamental human values which should form the basis of all bioethical reflection we should nevertheless have regard to those other cultural values upon which all societies are not necessarily agreed, learning to respect the way different societies do their ethics.

3.1.2. Eugenics

Eugenics, and with it notions of "superiority" and "inferiority" does not have to be applied to race. It is a mistake to identify eugenics only with racism (cf. Kevles, 1985). Eugenics stems from habits of mind, from the desire to protect "my group", and from a negative attitude to persons with physical or intellectual disabilities. Contemporary eugenics is generally not so much racist as it is connected with a desire to limit the number of people whose lives are held to be of such low quality that such lives, in terms of the burdens that they impose on societies as well as the affected individuals, are not worth living.

It is important to realise that scientific information in and of itself is never likely to significantly undermine race as a political category or eugenics as a political and social movement. It is also naive to imagine that scientists as scientists cannot be racist, eugenicist, or paternalist.

The danger is that genetic findings may be inflexibly interpreted as the only story of human, biological, and cultural evolution. In the first decades of this century, the racial hygiene movement, relying on eugenics based on a mistaken science, proposed negative attitudes to whole groups of human individuals. By the middle of this century eugenics has fallen into disrepute. But today, increasingly more strength is being given to genetic explanations of human behaviour, as can be seen in the scientific and popular press over the past decade (Nelkin & Lindee, 1995).

Eugenics can and is practised within a population precisely on the basis of "genetic reductionism", that there are some lives which, it is popularly claimed, constitute a burden to the community, to the individual concerned, to that individual's family, and whose quality of life is so low that these lives are not worth living. Such eugenics has nothing to do with race, but is based upon disability.

The problem is that in the way that the argument is expressed there is an underlying assumption that genetic differences between individuals constitute a rational basis for labels of 'superior' and 'inferior'. The point is that eugenics is built upon an attitude that seeks its justification in science, just as racism is an attitude that may seek its justification in science. These are habits of mind and ways of thinking philosophically that are hostile to the key notion of the inherent dignity of the human individual and the inviolable and inalienable human rights that arise from the international consensus about the value of human beings. Human value does not change according to sex, race, theories of

personhood, or any other factor.

With both eugenics and racism we are dealing with political and social constructs and not scientific categories. Eugenics may also be linked to distaste of persons with disabilities, to Nietzsche's idea of the threat that the disabled and chronically sick pose to the healthy (Nietzsche, 1910), and to the economic burden on the community which comes from the provision of longterm care for the disabled, the elderly, and the chronically sick. It is very important to realise that scientific information, in and of itself, is never likely to significantly undermine race as a political category or eugenics as a political and social movement.

We should not have the misconception that eugenics is a thing of the past, although, in present times, eugenics may express itself in not so obvious ways. For example, there are cases where insurance companies have cancelled policies of families who include a member found to have a genetic risk factor for a disease. This has been called genetic discrimination (Billings, 1992).

It should also be noted that present day eugenics has been expressed at the level of national government policies. For example, the population policies of the Singapore government is guided by eugenics: women who graduate from universities are encouraged to bear more children in the belief that their children have higher "intelligence", while lesseducated women are offered disincentives to have more than two children (Chee & Chan, 1984).

It may be pointed out that the inclusion of a many groups of people as possible, including groups of persons at risk of eugenic discrimination or at risk of racism, could work against racism as the total human race will be represented in genetic maps and libraries, if we compare it to the situation where the human genetic map was only derived from one population. The concerns that persons who suffer from particular diseases have of discrimination increasingly voiced in relation to contemporary developments in genetics research. The UNESCO International Bioethics Committee report on genetic screening discusses some of these issues.

3.1.3. Stigmatisation

Stigmatisation occurs when population groups in which there is a high incidence of genetic disease are selected for scientific investigation. This usually attracts attention to their genetic differences. Care needs to be taken that targetted groups do not become stigmatised in some way simply because they are of scientific curiosity or because they are more frequently studied, and more is known, and thus seem to have a greater predisposition to disease. Such stigmatisation can lead to unjust discrimination.

It is not surprising that some people are suspicious of genetic research which appears to have selected them for scientific investigation. Understandably they can see a danger that researchers in these projects will target the most "interesting specimens" because they are a fading population group. Looking down the wrong end of a telescope at our fellow humanity can reduce small, vulnerable, and potentially voiceless groups to the curiosity value of "endangered species" whose inherent human dignity could be overlooked. The ideology of eugenics often has links with both handicaps and racism, and was boosted by Social Darwinism and genetic

reductionism (Kevles, 1985; Macer, 1990).

3.1.4. Genetic reductionism and Holistic World Views

"Genetic reductionism" is used to refer to the evaluation of individuals with reference only to their genetic inheritance. Western science has frequently sought to explain the whole by a greater knowledge, by a part that is deemed to be most fundamental. Some researchers, pursuing Darwinian theory, propose an explanation of human beings in their origins as well as their evolution by reference only to DNA. Individuals have been categorised according to specific markers of inherited susceptibilities. Whatever the theoretical and scientific benefits of such categorisations, research scientists must always have regard to a more holistic appreciation of human beings, considered both as individuals with an inherent dignity, and as communities living in a given environment and culture.

It is precisely at this point that the objections of some population groups to population genetics have been most forcefully articulated. It is a mistake to imagine, for example, that opposition to certain research projects is based upon misunderstandings and confusions about scientific aspirations, and how the scientific information will be used. It is much more fundamental than that. It is a clash of philosophy and cultural insight concerning our understanding of the origins of humanity, the responsibility of individuals and the safety of the community in terms of past, present, and future generations. For many indigenous peoples, the dignity of their ancestors are "in our blood, our hair, our mucus, our genes", accordingly some research projects are seen as an unwelcome interference "in a highly sacred domain of indigenous history, survival and commitment to future generations".

The categories of populations that are chosen include those that can answer specific questions related to contemporary 'ethnic groups', language groups and cultures. Populations that are anthropologically distinct, that are linguistic isolates, and those in danger of losing their genetic identity will be chosen, as well as populations that are dominant in particular regions. The dominant population groups have nothing to fear, however some members of minority groups are already at risk of ethnic attacks and are therefore sensitive to any information that could be misused against them. For example, if the genetic knowledge can be used to classify them as distinct, e.g. French have a gene to make them good winemakers and drinkers, it could become a point by which they are ostracised though, the information could also be used for admiration. The usual cause for loss of genetic identity is not racial cleansing but the genetic admixture caused by intermarriage between different population groups. We could also expect concern from those groups who are also physically threatened by attempts to eradicate them, such as Kurds in Iraq.

If genetic reductionism derives from a misunderstanding of science and is suggestive of discrimination against a "genetic underclass", it also represents a threat to those mythologies or cosmogenies which are different from the dominant world cultures. The sensitivities and legitimate cultural and social norms of particular population groups have to be respected and honoured in any population genetics research. One of the ways to address the concerns of groups of persons at risk of eugenic discrimination, or at risk of racism, is to have good communication with disability support groups and ethnic communities. For example, Australian aborigines have suffered racism since European colonisation of Australia,

and they have expressed concern that decisions about the research were made independently of them largely in the United States or Europe. The planners of population studies in general could counter these concerns and the risk of actual abuse, by including the indigenous peoples in the planning stages as well as in the ethical discussions of these studies. "The human rights of people in populations should be respected", and these people should be seen as "partners in the work rather than merely subject of it." (CavalliSforza, 1994).

One of the fundamental points of opposition of indigenous groups towards genetic studies of human history is that the results may contradict indigenous people's views of oral and traditional history, and the meaning of genes and genealogy. For example, Maori people have two words to describe the human gene, one meaning "life spirit of mortals (Iratangata) and the other genealogy (Whakapapa), which connects Maori with themselves and others (Mead, 1995). The gene and genome are not the property of individuals but rather are part of the heritage of families, communities, tribes and entire indigenous nations. In this regard the UNESCO position on the human genome being part of the common human heritage is more compatible with the views of indigenous persons, than the view discussed in the patent section of those seeking patents on genes.

One response to the opposition has been to place some distance between population genetics research and patents by asserting that patenting is not the primary purpose of such research, and that in the event that genetic products of the research are commercialised, financial benefits would be shared with the people from whom the genetic material originated. Although some have found this acceptable, others have pointed out that this only serves to incorporate indigenous peoples into a system that views living organisms and community knowledge as commodities which can be patented, 'owned', and traded.

The discussion on the ethical, legal, and social issues arising from human genome research reflects a particular worldview, which has arisen in the context of a world economy that is dominated by the multinational corporation's drive for profits. The wrangle over patents, for example, reflects this world view. Yet, an alternative world view is evident when researchers gather germ material from peasant farms and tropical rainforests, and acquire knowledge and expertise from indigenous peoples and peasants, without being asked a single cent in remuneration.

Indigenous peoples' organisations have begun expressing their own value systems and discussing ways of conserving and protecting indigenous knowledge and culture. In the process, they have opposed the patent system as being fundamentally in conflict with their own value system. One analysis refers to the indigenous value system as the 'cooperative innovation system', and that of modern science as the 'institutional innovation system', and calls for the recognition of the contribution and value of the former toward the world's food supplies, farming systems, and medicinal needs (RAFI/UNDP).

3.2. Bioethics and Genetics Education

Public understanding of population genetics requires bioethics and genetics education. Such education has universal support. The questions are: what?, by whom?, to whom?, and who pays? Bioethics and genetic

education has been called for also in the genetic screening report of the UNESCO IBC, and is consistent with the founding goals of UNESCO. Population genetics research involves contact with and sampling of different populations. This presents opportunities to involve researchers and participants in a two way process of education.

As discussed above, the researchers should involve local participants in the research. This presents a chance for advanced genetics training, and training in taking consent and consultation from participating groups of people, not a concept currently found in the local scientific or legal environment! Researchers should also develop collaboration in the international context. Indeed, the process of anthropological research actually involves education of the researchers in the local customs and beliefs, which can then be shared with the rest of the world in efforts to help understanding among peoples. In this way all can learn through research.

The people participating in the research will be able to learn of the reasons why the sampling is sought and of the research goals. They may be interested to meet people from out of their community, though the contact should not create expectations which cannot be fulfilled. There is the need to share results. Some representatives of indigenous populations, however, have expressed concern that they do not want to know the results of scientific studies that challenge their local understanding of history.

There is also the education of researchers during the process of the research negotiations and of the results of any investigations, of the attitudes of local groups and populations. The process of anthropological research actually involves education of the researchers of the local customs and beliefs, which can then be shared with the rest of the world in efforts to help understanding among peoples.

In this way all can learn through research that is entered into with a willing spirit to learn. There are further issues that need special attention for population genetics, especially those discussed in the ideology section above. Racism and eugenics are deepseated attitudes, often related to a desire to protect the power of "my group", rather than rationally arrived at positions. It is generally believed that the misuse of genetics also depends to some extent on the level of education of genetics that people have. If education of genetics, as well as the bioethical issues it raises, is increased, many hope this would reduce the tendency for racism. Contrary to this, however, in the first part of this century most educated biologists supported eugenic thinking (Paul, & Spencer, 1995). Some would maintain that social eugenic programs of that time were based on false genetic knowledge, however, either interpretation of history illustrates the power of education.

There is a need for public and student education. Advances in biology and medicine have generally led to pressure upon educators of how students can be prepared to face the ethical dilemmas that the technology often raises.

In school and university education during the 1960s to 1990s in many countries science has been taught independent of social or ethical values. However, science educators have discovered during the last two decades that the most efficient way to educate science is to discuss the science together with examples of technology and put the facts into the social context. This method of teaching is generally called the Science,

Technology, and Society (STS) approach (Ramsey, 1993). Bioethics is one part of the approach of STS. There are a diversity of views on how to effect efficient education of social issues and even the science itself (Waks & Barchi, 1992). However, the point is that students learn more science when it is combined with practical applications. The problem is that value education has also been abused in the past to promote discrimination, and the weight of the word "scientific" can make people believe that such a value is also scientific. There is a need to work on what can be taught, and to promote decisionmaking, and recognition of human diversity.

The funding of educational efforts obviously cannot be absorbed totally in the budgets of the population genetics research. Therefore, there should be some commitment of the funds to education found in the Human Genome Project research programs for ethical, legal, social impact and educational issues.

4. Conclusions

4.1. Summary

Recently research involving human subjects has become more regulated. In addition to international bodies such as UNESCO, or HUGO, and national funding agencies, there are already national laws in many countries to involve local research ethics committees, such as Institutional Review Boards (MacKay, 1993). Current population genetics research is under the oversight of different layers of control which vary widely around the world. Some research is only under the discretion of individual researchers, most seek consent from the persons who provide the tissue samples, and the international regulations on research involving human subjects are clear that informed consent is needed. Some funding agencies demand ethical review, such as NIHfunded research in the USA. Some universities in the world also demand ethical review, and the trend is to have more review. The HGDP being an international project will demand international standards of consent and confidentiality, which when appropriately implemented in the local situation will be at least as good as ethical guidelines for existing research.

In addressing the ethical, legal and social issues of human population genetics research, several points of principles need to be considered. The body entrusted with the responsibility of overseeing such research should include substantial and legitimate representation of the target populations. Indeed, a wide representation of people's groups should be included in all stages of population genetics research projects. Considering that the protection of the intellectual and cultural property rights of the sampled populations is a legitimate concern, specific mechanisms on how to protect these rights ought to be formulated. Furthermore general statements of possible benefits flowing from research projects to local populations, such as the HGDP's claims that it will lead to the development of scientific laboratories in local areas, should be formulated concretely and specifically so that it becomes obvious how this will happen.

UNESCO International Bioethics Committee needs to consider whether they should outline some principles of ethical guidance, and give further explanation of practical measures and procedures. As has been pointed out

by Majumder (1995), Indian coordinator of the HGDP, in some countries the positive image of a UN body such as UNESCO would ease the concerns of local politicians and groups if they were to take a direct interest in the oversight of the HGDP. In fact as we observed during the consultation process during the drafting of this report, some researchers and some population groups have asked UNESCO to review the ethical issues, and to establish a committee to continue the ethical review of the research, and proposals. However, this would require the development of more detailed guidelines addressing the ethical and commercial issues raised by the HGDP. Such guidelines would also be useful for general population genetics research.

The broad involvement of UNESCO, WHO, CIOMS, HUGO, ICSU, and possibly other bodies within the regulatory committee is important. There is a need to include representatives of people's groups in all stages of population genetics research projects, and in the oversight committee. In North America the HGDP committee has included two representatives of indigenous peoples groups, and this should happen in a global sense, though we must ask who are suitable representatives. The answer to this may depend on the locality and situation, and should be flexible.

Regarding the HGDP, the scientific goals are generally valid, and the HUGO HGDP committee has produced a good introductory report on the reasons for the HGDP (HGDP Summary Document, 1994). The North American HGDP regional ethical committee has produced detailed guidelines, which has progressed the ethical review of future population genetics studies conducted within their auspices (Greely, 1995). The ethical guidelines do take account of the critiques of most writers, however, we can say that the organisers would have received less critique if they had more actively involved leaders of indigenous people's groups in the planning of the project. Indigenous people's organisations have opposed the HGDP on several bases, a fundamental one being that while many groups of indigenous peoples face physical and cultural extinction, the project has not expressed concern about their eventual disappearance, but has instead expressed urgency in collecting tissues from these groups before they disappear as separate entities. The ethical oversight committee of the HGDP should address this issue in concrete ways, perhaps establishing that a portion of research funds be set aside for indigenous people's efforts to protect themselves.

The goal of population genetics to understand human history is controversial because of feared misuse, but the possible medical goals seem to be universally accepted except for the fact that the medical techniques may be patented. The possible patenting of products from the material collected from sampled populations has given rise to concerns that financial benefits are derived from them but will not benefit them in any way. These concerns are based upon their past experience in having had their knowledge of medical plants appropriated by outside parties. Cell lines and DNA collected during population genetics projects can be a potential target of commercial researchers, as shown in several patent cases. Although some researchers, and the HGDP has committed itself to protecting the intellectual property rights of the sampled populations, the mechanisms for doing so are not clear, and it is extremely difficult for anyone to be in a position to guarantee that others cannot commercialise research in the future.

The goal of reducing racism is the most debatable claim of the HGDP, and it will be impossible to provide any proof that it will or will not

happen until after the event. Careful attention must be made to these concerns.

However, there is no reason to believe that the HGDP will make it worse than other population genetics research, in fact the additional regional ethics committees of the HGDP have the potential to better safeguard the participants than the research conducted independently as done in the past. At an early stage in the project's planning, several groups speaking for indigenous peoples called for a halt to the Project. However, it would seem to be impossible to stop the general progress of this project, and it is not within the mandate of UNESCO to call for a moratorium on such a project or on population genetics research. The response of UNESCO has been to ask other groups to join in the regulation of population genetics, and the HGDP. This invitation should be formally extended to members of indigenous groups to join the ethical oversight committee of the HGDP. These principles apply to population genetics in general.

The use of research results should in no way harm persons and not result in possible discrimination of the individual and population concerned. Future increased ability to identify people genetically at risks for genetic and common diseases, needs to be accompanied with the measures to protect the individual from stigmatisation and misuse of information by a third party. The same applies to process of genetic screening on the population basis, as well as of genetic screening on individual levels (Note: we rely on the 1994 UNESCO IBC report on genetic screening, and the 1995 UNESCO IBC report on genetic counseling).

4.2. Sanctions

While as described earlier, regulatory oversight usually foresees a certain degree of scientific and ethical review prior to acceptance of a research protocol, once accepted, ongoing monitoring and surveillance usually are not assured. Even less certain is the possibility of sanctions in whatever form. Disciplinary measures including for example, suspension, withdrawal of privilege and fines, constitute the usual avenue of professional measures. In addition, where research subjects have been harmed, civil and criminal sanctions are also possible. Funding bodies may withdraw funds and sometimes even retroactively. The latter is rare however. In any event, unless involving great numbers as in the HIV blood testing scandals and the recent breast cancer trials, cases of research fraud or of failure to respect basic ethical norms are usually not brought to public attention.

If researchers are to become more accountable and actual practices more transparent, other forms of sanctions or at least of publicity (through a "black list"), should be envisaged. Stricter, standardised reporting requirements, on a regular basis and publication of such reports are one such avenue. We consider the latter to be a basic ethical obligation that should be universally applied.

If researchers are to be subject to greater scrutiny, the same holds true for the media whose duty of honest, scientific reporting and preservation of privacy needs to be underscored. Whole populations, communities and the researchers themselves have often been wrongly depicted and wrongly represented with the resulting unjust labelling and discrimination. Such practices only serve to undermine public confidence and participation in research.

4.3. Conclusions

The scientific and philosophical traditions that have long permeated research are also present in population genetics. The prevailing attitude in science is that research is in and of itself a good. Therefore, if properly explained and understood, participation should be forthcoming. Communities and populations however, have their own cultural traditions and histories that need to be understood and respected. Moreover, population genetics is not simply a multiplication of the individual ethical and legal issues already raised by genetic research. There are different concerns and traditions in each group under study, and even among individuals within any group. The degree of information, consultation and cooperation must reflect such differences in participants. Likewise, the role and responsibilities of the researchers and of the local and national authorities, as well as the societal implications, will differ.

Having examined then, the ethical issues particular to population genetics, their philosophical basis, their research methodologies and possible utilization of research results and most importantly, the need for education because of fears of identification and stigmatisation through selection, of discrimination through participation, and, of possible eugenics through interpretation, we have recommended in this report the following issues as crucial to ethical review of population genetics research at institutional, and regional or global levels.

(*To add 1 sentence summaries of the following 19 points? Any more??)

- 1) accessibility to populations;
- 2) consultation with populations;
- 3) individual and group consent mechanisms;
- 4) ongoing ethical review;
- 5) inclusion of representatives of populations in decisionmaking;
- 6) communication, education, benefits, and feedback strategies at the population level;
- 7) confidential data and sample banking;
- 8) continual scientific review and monitoring and finally;
- 9) appropriate sanctions.

At the last session, the IBC was requested to consider establishing a committee on the ethical questions that might arise in the HGDP. This proposal has been supported by WHO, CIOMS, ICSU, and HUGO. We recommend that such a committee should be more broadly conceived so as to be available for ethical consultation for all human population genetic research projects, and not only the HGDP. We do not think that UNESCO should endorse any particular research project, but a committee should be made available for consultation when sought. In this way the independence, neutrality and credibility of UNESCO will be safeguarded. Given the concern shown about population genetics and in particular for the HGDP by indigenous peoples' organisations, we strongly recommend their inclusion in such a committee.

We suggest the following paragraph could be added to the preamble of the UNESCO Declaration on the Human Genome and its Protection in Relation to

Human Dignity and Human Rights:

(**To be written?? Bearing in mind that human cultural and genetic diversity is an intrinsic value of the human race...)

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