Commission on Intellectual Property Rights

Study Paper 10

Human Genome Patents and Developing Countries

Sivaramjani Thambisetty

Exeter College
University of Oxford

CONTENTS

METHODOLOGY:

The following specified terms of reference have been used as a guide to address issues under several broad areas.

1. *How widespread is the patenting of human genetic material derived from developing countries, or relevant to them?*

2. *Should there be prior informed consent, from the people donating genetic material, to patents being sought for that material or products derived therefrom?*

3. *Is it sufficient to obtain the consent of the person donating the genetic material or should consent be obtained from others sharing characteristics of the material?*

4. *What provisions should there be to ensure that donors of the original material or a group to which they belong share in any of the benefits arising from any patents on that material or product derived therefrom?*

5. *Should the patent laws in developed countries play a role in enforcing any requirements relating to prior informed consent or benefit sharing?*

6. *Should the original donors of genetic material on which patents are based have any influence on how those patent rights are exploited?*

7. *Do any developing or least developed countries provide or plan to provide patent protection for human genetic material. If so, what is the rationale for providing such protection?*

8. *Do current practices in the developed countries in relation to the patenting of human genetic resources raise any other issues for the people of developing countries?*

Secondary published data was used in writing report, as well as some original empirical data. An attempt has been made to critically present the main streams of thought in the literature, as well as detail legislation and regulations available in various countries. Where patent systems in developed countries are discussed, reference is mainly made to United States law and European law. All sources have been acknowledged and extensive notes provided. Recommendations are made on the basis of information and analysis presented in the following pages.

EXECUTIVE SUMMARY

There is an international consensus among countries, reflected, among other things, in the UNESCO Declaration on the Human Genome and Human Rights, 1997, that human genome sequence information should be freely available. This would ensure that important research is carried on without restriction in developed countries as well as in those developing countries with the means to do so. However, developments in patent law have meant that human gene sequences are being patented, raising the spectre of restricted access to such information as well as high prices of any useful products developed. There is a need to clarify what information on the human genome is freely available, and to what extent national patent systems should be allowed to impinge on the international consensus.

It is recommended that the relevance of the UNESCO Declaration on the Human Genome and Human Rights be re-evaluated. The Declaration also states that the benefits derived from knowledge about the human genome should be shared by all countries. Merely making the genome sequence itself available freely on the internet for example, satisfies this principle only in letter and not in spirit. The situation should be clarified with respect to industry expectations of patent protection as well as developing country expectations about public health improvement. It is recommended that gene sequences should remain pre-competitive information so that greater quantum of research and analysis can be carried out in the post genome sequence phase.

I. The possibility and implications of patenting of human genetic material taken from developing countries:

The following question was used as a guide to this section:
How widespread is the patenting of human genetic material derived from developing countries, or relevant to them?

The patenting of genetic material is a matter of relevance for all countries, developing and developed, because of the public health implications of advances in biomedical technology as well as due to rights implications for the human participants in such research. For many reasons, developing countries present ample scope for genetic research, both population genetics as well as study of individual genetic make up. But proposals for such study have been greeted with caution and suspicion by most developing countries. These responses have come from both, 'vulnerable' groups within developing and developed countries as well as national governments of developing countries. This has largely taken the form of indigenous peoples declarations, and regulations that govern international collaborative agreements as well as protect the subjects of such research. This is a reaction to a common perception that such studies may lead to unethical collection of genetic material as well as result in profits and medical advances that the participants in developing countries will not have access to.

Oversight of the compliance of such regulations in developing countries is difficult without control over researchers who may be based in another country. To aid developing countries oversee enforcement of local laws; it is recommended that patent applicants be asked to mention the source of human genetic material. Also it would be

useful to have such information indexed in patent databases so that at the very least, country of origin of the human genetic material can be flagged and used as a basis for policy formulation.

II. Patenting and informed consent of participants in genetic research:

The following question was used as a guide to this section:
Should there be prior informed consent, from the people donating genetic material, to patents being sought for that material or products derived therefrom?

Genetic material is a special case for the patent system in many ways. The information is personal; knowledge of which conveys information about the person as well as of family members and other people who share the genetic characteristics. More importantly for the patent system, is the dual nature of the material. It is both tangible material as well as intangible information. The patent system while protecting the information in the genetic material dissociates the human source of the material from the invention itself. Hence, critics who speak of the rights of the human source of genetic material, and the proponents of the patent system seem to speak past each other.

The relationship between the person and her genetic material that may become part of an invention can be viewed from personal rights as well as a property perspective. Both seem to imply informed consent of the participants in genetic research as essential, which process, it may be argued, is incomplete without information about possible commercialisation of the results of the research. Informed consent of a research participant is a well-recognised international principle. It is recommended that further steps should be taken to make this an unambiguously binding legal principle. Such a step would increase the confidence of developing countries and ease international collaboration in genetic research. Article 3 of the European Charter, is a step in the right direction, but this too, falls shy of mentioning informed consent in the context of patenting.

III. The relevance of community consultation and consent:

The following question was used as a guide to this section:
Is it sufficient to obtain the consent of the person donating the genetic material or should consent be obtained from others sharing characteristics of the material?

Group consent has been recognised as necessary in case of certain genetic studies by some international bodies, including the International Bioethics Committee of UNESCO. It is a complex requirement that is compounded by the heterogeneity of the groups that could potentially take part in a genetic study. Communities should have a chance to assess the benefits and risks of taking part in such research; this process is necessary for their self-determination, much like an expression of personal autonomy in individuals. Community consent is particularly significant because of the negotiating point it represents for the community. But group consent is not a substitute for individual consent.

This section describes various international and national efforts to ensure community participation in an informed way in genetic research. If compliance with such guidelines is essential to conduct the research, then there is every reason to include the process of

commercialisation within the scope of this process. Linking ethical guidelines with commercialisation of research will strengthen protection of community rights. One way of doing this is to initiate international guidelines that researchers and patent systems must respect.

IV. Benefit sharing with the research participant:

The following question was used as a guide to this section:
What provisions should there be to ensure that donors of the original material or a group to which they belong share in any of the benefits arising from any patents on that material or product derived therefrom?

The international guidelines and national regulations in this context highlight certain core tensions. Promising a share of the benefits to a potential participant in a genetic study seems to contravene ethical principles that the body or the human genome in its natural state should not give rise to financial gain. The ethical validity of consent that is given under the promise of benefits to be gained is also questionable. Given this, many guidelines specify a gratuitous model for use of human genetic tissue. However, such a model, as evidenced by developing country regulations is not a model of choice for many reasons. Many developing countries' regulations specify benefit sharing in the form of technology transfer, medical benefits or a share in intellectual property rights. This finds support in the UNESCO Declaration on the Human Genome. In this context it is recommended that international measures of benefit sharing should be undertaken in addition to the national regulations. One such measure was suggested by the Ethics Committee of the Human Genome Organisation; that commercial entities that benefit from biomedical research in developing countries should consider contributing 1-3% of their profits towards humanitarian measures. It is recommended that the bioindustry should be consulted on the feasibility of such measures.

V. Patent laws in developed countries with respect to informed consent and benefit sharing

The following question was used as a guide to this section:
Should the patent laws in developed countries play a role in enforcing any requirements relating to prior informed consent or benefit sharing?

The question of whether the patent system should be concerned with matters external to actual patentability criteria is a deeply divisive one. There are those who feel that certainty in patentability standards is crucial for the maintenance of the bioindustry's prospects and additional requirements like informed consent or benefit sharing will entail high transaction costs and are not called for, given the nature of a patent grant. On the other hand, the patent is the fulcrum of the process commercialisation of biological and genetic resources, and critics have expressed concern that the patent system may be rewarding unethical behaviour on the part of patent applicants.

There are two main reasons, as evidenced by the literature, why it may be argued that informed consent should be enforced via patent laws. The Convention of Biological Diversity is a binding legal document and it calls for such measures. If informed consent is required for the taking of plant and animal genetic material or traditional knowledge, there is reason to believe that informed consent should be necessary for taking of human

genetic material as well. International regulations and the wide acceptance of informed consent in national legal systems add weight to the argument that informed consent should be regarded as a binding norm in international law. No state can license an agency (the patent office) to reward inventors who may have violated such a norm in developing their invention.

A certificate of compliance as part of a patent specification that all national laws regarding informed consent and benefit sharing where applicable were obeyed, may be one way of incorporating such norms. It is generally accepted that research without informed consent is unethical. Where such consent has been taken, the information maybe inserted into the patent without great additional cost. Where informed consent was not taken it will act as a deterrent to unethical behaviour.

VI. Post grant control over use of a patent:

The following question was used as a guide to this section:
Should the original donors of genetic material on which patents are based have any influence on how those patent rights are exploited?

Some commentators draw arguments from notions of human dignity to maintain that a person continues to have a strong interest in how human genetic material taken from her is used, handled and commercialised. From this flows the position that the original source of genetic material on which patents are based should have an influence on how patent rights are exploited. If such a claim is recognised, it could lead to uncertainty in how patent rights are exercised. However, if informed consent to commercialisation has been taken and benefits sharing agreements entered into, then this question of post grant control over patents may not arise. This is can be seen as another reason why it would be in the interests of patent applicants to comply with such regulations at the time of conducting the research itself. It is recommended that institutions like Medical Research Councils should encourage researchers to follow ethical standards comparable to the researchers country of origin while conducting research overseas as well as follow regulations at the site of research.

VII. Developing countries and patent protection for human genetic material:

The following question was used as a guide to this section:
Do any developing or least developed countries provide or plan to provide patent protection for human genetic material. If so, what is the rationale for providing such protection?

A study of patent laws in many countries shows that no country allows for the patenting of human gene sequences, unless technical contribution has gone into it. Information collated from a WIPO questionnaire on the subject shows that this is true for most developing countries as well. Colombia, Cuba and Brazil have indicated that human gene sequences may not be patentable in their countries. There is a wide variation among developing countries as to the impact of human genome studies. India, China, Brazil and South Africa for example have the infrastructure to make use of freely available genome sequence information for their own priority research areas. The question whether developing countries will be able to exclude patents on human gene sequences at all under the TRIPS agreement is discussed in this section.

In this context it is recommended that where patents are taken out on human gene sequence information that is of particular public health relevance in developing countries, a research exemption should apply in a way that is broader than that applied in developed countries. This would allow those with the means to carry out such research in developing countries to continue to do so. Also, public health needs of developing countries maybe best met by technology transfer to the more advanced developing countries who can then prioritise resources for this.

VII. Other issues raised by the intellectual property protection for human genetic resources:

The following question was used as a guide to this section:
Do current practices in the developed countries in relation to the patenting of human genetic resources raise any other issues for the people of developing countries?

There are three significant effects of patenting of human genetic resources described here that may impact on developing countries. The first is that the secrecy and strategic behaviour associated with patenting of such knowledge may undermine the norms under which academic information is freely exchanged. The basic science infrastructure in developing countries, which is very important for the biotechnology industry, may suffer as a result of this. Secondly, it should be recognised that the human genome project has the potential to widen the 'apartheid' in health care between rich and poor countries by leading to greater individualised care for those who can afford it. The relevance of the scientific advances represented by the mapping of the human genome must be maintained for both developed and developing countries. This requires that medical researchers be encouraged to seek interventions that are population based and emphasis is put on developing inexpensive drugs and vaccines that prevent disability and disease in populations. Thirdly, there is a likelihood that some laboratories maybe conducting research into the genetic resources of poor populations in places akin to 'experimental havens' by analogy with 'tax havens' because of inadequate regulations on ethical research or difficulty in overseeing compliance in the case of foreign research collaborations. International initiatives may be need to prevent such a situation. It is recommended that the country of origin of the researcher should also enforce ethical standards comparable to such country's standards when overseas research has been authorised.

RECOMMENDATIONS

A. The link between intellectual property rules and ethical regulations over genetic research should be institutionalised. Human genetic research is highly international and interactive in character, hence agreeing on standards for informed consent and benefit sharing present a regulatory challenge akin to those that deal with genetic resources under the Convention on Biological Diversity.

B. Specifically, it is recommended that steps be taken to recognise informed consent of individuals and groups where appropriate, as a legally binding principle that should be appropriately complied with during all human genetic research.

C. A certificate to the effect that informed consent was taken from participants, that local laws and regulations were obeyed, as well as specifying their origin and location, where appropriate, should be appended to all patent applications that describe inventions that comprise human genetic information and the products derived therefrom. Such a certificate of compliance can be included with relative ease where informed consent has been taken, and will act as a deterrent to unethical research. Such a measure would increase the confidence of developing countries to initiate greater research collaboration with foreign and international entities.

D. Where such compliance cannot be assured, there should be provision for sanctions within the patent system.

E. There are circumstances when samples are anonymised or informed consent is not possible because samples were collected previously. Allowance for such cases should be made. In this regard national bodies like Medical Research Councils or Genetics Commissions should be consulted.

F. It should be recognised that the biomedical advances represented by increased knowledge about the human genome must be shared between all peoples in developing and developed countries.

G. One way to do this is to recognise the need for benefits sharing agreements when people from developing countries participate in genetic research. Such measures may include technology transfer, medical services or a share in intellectual property rights for the collaborating site in the developing countries. It is recommended that profit making entities, including academic institutions, be encouraged to commit a percentage of their profits from genetic research to humanitarian work in the developing countries involved.

H. The benefit sharing should extend to public health advances. Special measures should be taken to identify diseases and disabilities that are the largest afflictions in developing countries. It is possible that the human genetic sequence or the sequence of the pathogen involved may already be patented. In such cases, the possibility of providing special research exemptions under patent law for such studies should be explored.

I. It is possible that basic science in developing countries is adversely affected by failure or delay in publishing of scientific papers because they describe results or ideas that could give rise to a patentable invention. Given that basic science infrastructure is essential for biotechnology industry, it is recommended that this issue should be investigated further. Supporting scientific advancements in developing countries will help in developing biotechnology that is specific to their needs.

J. It is recommended that, once a patent has been granted, the original sources of the human genetic material should not have control over how it is exercised under patent law itself, as this would bring about uncertainty of control. Such control may be exercised through contractual agreements, and should be decided before the research is conducted.

K. In order to help in evidence based policy making, it is recommended that patent information services be developed that index the location and people from which human genetic material was taken, keeping in mind requirements of confidentiality of such participants where appropriate. Patent applicants should be asked to provide such labels for their research that can then be used to gauge what kind of research is being commercialised, and where it is being done.

L. International initiatives are required to evaluate the relevance of the notion that human genome sequence information should be made freely available to all. If this information is not regarded as pre-competitive information, then global health advances may slow down, and become too expensive to be of real benefit to peoples in the developing world.

M. The way in which national patent systems in developing countries impinge on the international consensus that human genome sequence should remain accessible, should be investigated. One way of reversing the trend is not to allow product patents on the DNA sequence itself, but only *use claims* on resulting end products. It would be detrimental to useful research to allow the patentability of human gene sequences whose function is known only through use of bioinformatic tools. It is recommended that one possibility is to put in place subject matter limitations that were an important part of patent law till recently. Specific subject matter inclusions or exclusions will allow for policy based decisions on what may be patentable and what may not be. The current system whereby the scope of what is patentable changes incrementally and in undirected ways is too problematic. It is recommended that industry and academic institutions be consulted on a continuous basis, as to what their reasonable expectations in this respect are.

N. National patent systems are dealing with human genome information which is a finite resource and is the common heritage of humanity, albeit in a ‘symbolic sense’. Given the international nature of genetic research and its global relevance, the role of domestic patent systems should be seen as one that is of significance for both developing and developed countries. Public health interests, should ideally transcend national boundaries, and should be taken into account when evaluating the pros and cons of any action taken by national patent systems.

DEFINITIONS USED IN THE REPORT:

Human Genetic material: *In this report human genetic material refers to material derived from any tissue samples that can serve as DNA sources; including not only solid tissues, but also blood, saliva and any other tissues or body fluids containing nucleated cells from which DNA can be isolated*[1].

Source of the human genetic material: *The term 'source' here is used as the most appropriate and in order to refer to a wide range of circumstances under which people provide tissue samples. It is especially inappropriate to use the term 'donor' which may imply an 'intent to make a gift or to relinquish control that may not apply to any particular individual'*[2].

Informed Consent: *Consent is informed when it is given by a person who understands the purpose and nature of the study, what participation in the study requires the person to do and the nature of the risk and what benefits are intended to result from the study*[3].

INTRODUCTION

The patenting of human genetic material is of considerable importance to all countries; developed and developing. In recent years intellectual property protection has emerged as one of the most significant areas of conflict between developing and developed countries. This is due to the projected international harmonisation of patent standards and its linkage with trade issues via the TRIPS agreement[4]; However, the patenting of human genetic material has been particularly controversial.

Patenting of human genetic material became controversial primarily for two reasons; the need to keep raw human genome data freely accessible and the question of human genome diversity studies and medical advances derived therefrom. This last issue is of special relevance to developing countries. Genetic studies exemplified by the identification and sequencing of the human genome, has been described as the search for '..complete knowledge of the organisation, structure, and function of the human genome – the master blueprint of each of us…'[5]. In less rhetorical but no less startling terms, the ultimate goal of such a search is to better human health through science. Some of the projected benefits of sequencing and post sequencing analysis include the diagnosis of genetic diseases and development of gene therapy[6]. But there is concern that the full benefit of the medical advances that may result from decoding the human genome will not be realised if the genes become subject to privately owned intellectual property and are exploited for profit. This is a concern that is shared across developing and developed countries[7], but felt more acutely by developing countries.

An international consensus has emerged that raw human genome data should be kept freely accessible. This has been a point of contention ever since the launch of the Human Genome Project, and certainly much before the joint statement of Blair and Clinton in March 2000 where they said that 'raw fundamental data on the human genome, including human DNA sequence and its variations, should be made freely available to scientists everywhere'. Following a fierce dispute, the data on the human genome has been published on the internet to make it accessible to scientists everywhere. Celera Genomics, a private corporation based in the USA provides the same data for a fee claiming that it provides value addition to the data. (See Box 1, Table 1).

Apart from this issue of access to the genome data, patenting of individual sequences has led to severe controversy. Technology that made the human genome sequencing possible allowed for the rapid isolation of gene sequences without full knowledge of functional aspects. If these sequences are then patented, (provided they fulfil patentability standards) subsequent functional work on the gene sequences will be controlled by the original patent holder whose inventive contribution in sequencing the gene itself is slight. This aspect of the patentability debate is most prominently voiced over patentability of Expressed Sequence Tags or ESTs. The debate was triggered in 1991 with an application by the NIH in the US for 6869 sequences, which are partial or full-length cDNA sequences with as yet unknown functions. The application was subsequently withdrawn, but not without general concerns being raised by the scientific community, as well as industry on the possible negative consequences for research, development and international co-operation[8].

This controversy is still alive, more recently because the human genome is now known to have about 30,000 genes and not the previously estimated 100,000 genes[9]. This new revelation means that one gene may be transcribed in a number of ways, so that the link between a sequence and the associated proteins must be much more complex than previously realised. This calls for greater work on the functional aspects and raises the possibility that as the science develops, we will understand more about sequences that may have already been patented. The statement of the Human Genome Organisation in 1992 about ESTs that 'at this stage, any monopoly would reward those who make routine discoveries, but penalise those who determine biological function or application' has never been truer.[10]

In this context, UNESCO sought to bring some level of international consensus on how information about the human genome should be handled. The first article of the Universal Declaration on the Human genome and Human Rights adopted by the General Conference of UNESCO in Nov 1997 refers to the human genome as the heritage of humanity *in a symbolic sense.* It also says in Art 4 that the human genome in its natural state shall not give rise to financial gain. Unfortunately, these statements have not had much effect in practice with respect to what can and cannot be patented in most developed countries. There is a sense in which the patent system in Europe and the USA seem to reflect these principles in a mere 'symbolic' way[11].

Human gene sequences in their natural state cannot be patented; this is true in all patent systems. However, in real terms this statement has not been regarded as a fundamental barrier derived from the justifications for patent grant, but rather as an inconvenience to be overcome. The broad principle on which this statement is based is the dichotomy between discoveries, which cannot be patented, and inventions, which can be. Under both US and European law, substances that are naturally occurring are patentable if they have been isolated and purified and made available in a form in which they were not previously available. The key is an evaluation of 'human intervention' in the US and 'technical contribution' under European law. In the context of human gene sequences, often this qualification to the 'discovery-invention' dichotomy has meant that human gene sequences are patentable, provided they fulfil the criteria of patentability.

Therefore, currently, given that patent applications based on genomics normally claim isolated DNA sequence and its variants as well as other aspects, the significance of efforts to keep human genome data freely accessible is unclear. It either refers to a *mere* ethical approach to resist the commodification of human genetic material, or it refers to the free availability of the public human genome sequence database referred to earlier. Admittedly, the patenting of human genes has been going on for sometime before the launch of the human genome project. It is estimated that between 1981 and 1995 a total of 1,175 patents for human DNA sequences were granted worldwide[12]. But the current tension is heightened because of the consensus that human genome data should not be appropriated, and the nature of patents that are being granted which seem to disregard the consensus.

To illustrate, The DNA sequence based applications being filed in the European Patent Office can be described as falling into three categories. The first being classic ESTs, which are short partial sequences accompanied at best by a tentative indication of the nature of the encoded protein based on similarity to known sequences. The second category is used to describe a sequence, usually but not always a full length one, for

which a possible function or use for the sequence or encoded protein has been assigned solely on the basis of bioinformatic data. The third refers to full length DNA sequences encoding proteins with a proven function or use established by experimental data.[13] It is as yet unclear whether patents will be granted for these 'inventions'. The new Utility Examination Guidelines of the US Patent and Trademark Office imply that it will require a specific, substantial and credible utility[14]. There are indications that the kind of workable standard this refers to is not a very high one. The US Patent and Trademark Office has already issued one patent on partial sequences whose function is known only through homology[15]. This class of patent applications is referred to by a member of the EPO as most problematic of all DNA sequence based inventions[16].

The present situation is very confusing. Either it should be acknowledged that industry expectations are such that nothing less than patents on human genomic sequences will be acceptable to the biotechnology sector or genomic sequence information should be freely available in effect and appropriate patentability standards should be adopted. The issues are obfuscated largely because of the rhetoric about keeping genomic sequence information freely available, when in effect it may not be. In this context, it is suggested that the continued relevance of the UNESCO declaration, if any, should be studied.

Various critics of the patent system have proposed alternative approaches. One significant way seems to be that patents should no longer be granted for DNA, but only for clear functional applications that are end products. This implies that there should be no more product patents on the DNA sequence itself, but only *use claims* on resulting end products. This would safeguard genes from any kind of appropriation, but would probably be objectionable to the biotechnology industry, as a traditional product claim on DNA offers broader protection than a specific *use claim* on DNA, as the latter will mean the patent holder does not have rights over *every* possible use and *every* possible application[17]. The biotechnology sector must be consulted on this matter, including academic institutions that are key producers and users of information in this sector. It should be recognised that interests in this issue are not homogenous across the entire industry[18].

As the data in Table 1 shows, access of developing countries to human genome sequence data in the public domain is clearly not on a competitive level with other locations of genetic research. Even within developing countries, the impact and relevance of the scientific advance represented by the mapping of the human genome varies. According to the WHO health report for 2000, there are enormous differences between developing countries in burden of disease, financial resources, and educational attainment and health systems.[19] Countries like India, Brazil, Indonesia and Korea have biotechnology industries capable of producing new and high quality, low cost generic drugs. Vietnam, South Africa and China are endeavouring to produce their own essential vaccines, in the face of competition from multinationals[20]. Already new vaccines are under development that has been directly derived from the DNA sequence of the pathogen involved. But 'whether and how fast vaccines are developed will depend on the rich countries and those with means in poor countries'[21]. In this context it is especially important for developing countries with mature biotechnology industries and R & D potential that 'DNA molecules and their sequences, be they full length, genomic, or cDNA, ESTs, SNPs or even whole genomes of pathogenic organisms, of unknown function or utility, as a matter of principle, should be viewed as part of *pre competitive information*[22]. This will help developing countries that have the

infrastructure, to undertake genetic studies on their own. It is recommended that special studies be conducted to identify key technologies in the developed world that have already been patented and are of particular relevance to developing country public health needs. Measures like technology transfer and special research exemptions should be considered for such inventions.

BOX 1

It has been suggested that the internet could turn out to become the equaliser in the brave new world of research into human genetics. But only upto a point.[23] It is claimed that data supplied by the Britain-based Human Genome Project is being studied significantly by scientists in the developing world in search for new medical treatments. The Human Genome Project data is updated every 24 hours and available on three major websites in Britain, United States and Japan. But often, access to this by developing country scientists may not amount to a lot in relative terms. The tables A and B below show the number of times a relevant website was accessed by entities based in different locations. The website is www.ensemble.org maintained by Ensemble, a project run jointly by the Sanger centre and the European Bioinformatics Institute to provide annotation of the human genome sequence and bioinformatics tools for interrogating and using the data. The data shown in Table 1 represents a weekly average for the year 2001 ending with the second week in November. Table A shows that the volume of hits from the developed world is vastly higher than the number of times of access from developing country locations. The data is another indication that the developed world is better equipped to research into the human genome. This coupled with the patent system, as pointed out by Dr Cameron, Director of the European Bioinformatics Institute, could mean that multinational companies in the developed world would take out the bulk of patents on the freely available data[24].

TABLE 1 A

Domain Suffix	Location of Access	Number of times accessed per week
uk	United Kingdom	59951.6
edu	U S Educational	49420.0
com	U S Commercial	40344.9
net	Network*	31302.4
de	Germany	23640.9
fr	France	19464.3
org	Non-profit Organisation*	7634.7
nl	Netherlands	6716.9
ca	Canada	3923.1
gov	U S Government	3825.2
es	Spain	3723.9
dk	Denmark	1472.6

* Non country specific domain suffixes.

TABLE 1 B

Domain Suffix	Location of Access	Number of times accessed per week
za	South Africa	724.24
br	Brazil	465.62
in	India	230.2
ar	Argentina	175.15
cn	China	111.02
co	Colombia	79.02
tr	Turkey	58.35
ve	Venezuela	55.73
th	Thailand	50.60
ph	Philippines	14.95
pe	Peru	6.0
cr	Costa Rica	2.91
ec	Ecuador	2.15
bo	Bolivia	0.53

Data source: Web team, Wellcome Trust Sanger Institute.

1

THE POSSIBILITY AND IMPLICATIONS OF PATENTING OF HUMAN GENETIC MATERIAL TAKEN FROM DEVELOPING COUNTRIES

The following question was used as a guide to this section:
How widespread is the patenting of human genetic material derived from developing countries, or relevant to them?

1.1 Developing countries are specifically affected by patenting of human genetic material because of population genetics research. The Human Genome Diversity Project (HGDP) is one such that was launched as a response to the fact that a vast majority of detailed research into human genetics had so far been done with Europeans of North Americans of European descent and so omitted 80% of the world's population that is not of European ancestry. It is expected that greater knowledge about human genetic diversity will advance the study of those genetic diseases found largely in non-European populations and because genetic variation is basic to better understanding of a host of diseases found in all peoples[25]. Population genetics also aims to understand the working of human evolution better.

Isolated populations are the main source for observation of genetic forces acting in human evolution. Consanguinity and large family size are particularly interesting for such studies.[26] Because of these features, populations and groups in developing countries and indigenous groups within developed countries are interesting participants in such studies. A key scientist in genomic studies in India described why countries like India provide certain strategic advantages for human genome studies. The following statements, with some exceptions, are true of many developing countries. Firstly, India's large population and family size are ideal for genetic analysis. A considerable number of rare genetic disorders are likely to be found merely because of the population size. Secondly, the developed world, (unlike India), has eliminated a large number of genetic disorders by prenatal counselling; it is therefore likely that a number of genetic mutations are still to be found in (developing countries like) India. Fourthly, India has a large number of competent medical practitioners with modern clinical expertise and vast network of hospitals, clinics and health centres[27] that can provide a basis for such studies.

Similarly, China is thought to offer a particularly rich seam for genetic research because the population is relatively homogenous[28]. Given that research groups may find it profitable to conduct genetic research in ethnic or regional groups and populations in developing countries, many of these countries have detailed international research collaboration guidelines in recent years. Such regulations were updated or formulated in the aftermath of some well-publicised cases of appropriation of human genetic material from poorly informed indigenous groups.

In one such case blood samples were extracted from some members of the Hagahai, a small group of hunter-gatherers living in an inaccessible mountain range in Papua New Guinea. The researcher involved told the group that she wanted to see a

'binitang' – an insect – in their blood[29]. Analysis of these blood samples revealed existence of antibodies to a variant of the HTLV-I leukaemia virus. This was used to produce an immortal cell line, which was the basis for a patent application relating to the cell line, the infecting virus, and a set of ancillary diagnostic kits[30]. Attempts like these to patent genetic material came under severe criticism from many parts of the developing world. Table 2 is a list of statements from indigenous peoples who rejected the Human Genome Diversity Project in the immediate aftermath of the controversy[31]. This list can be seen as an indication of the sources of objections to the patenting of human genetic material. Those who oppose the Genome Diversity Project see it as objectification and commodification of human life. There is a common perception among such groups, based on the apparent insensitivity of the goals of such studies, that human beings will only count as objects of research and not as beneficiaries of scientific development. In this context, even though 'traditional peoples' may see the whole idea as a violation of the sanctity of life, it may be irrelevant if national governments do not share their view[32]. Therefore it is important to acknowledge that national government positions may not always reflect the wishes of indigenous groups within the country.

A large part of the objections to patenting of human genetic material that come from developing countries, like in the developed countries, focus in the alleged immorality of patenting material that derives from the human body. As the various declarations listed in Table 2 show, the concerns emerge from a different worldview of nature and culture than what the patent system is based on[33]. The perception of immorality is accentuated because of possible past colonial exploitation and a continuing loss of their 'resources' and way of life. The language used to describe the patenting of resources from developing countries, be it animal or plant germplasm, or traditional knowledge or human genetic material as 'bio-piracy'[34] is revealing of the nature of some of the objections. The patenting of human genetic material is thus a deeply emotive issue for many peoples in the developing world and governments have time and again raised the issue at various international forums.

To summarise, the concerns over patenting of human genetic material of the peoples of the developing countries can be classified into three types. Firstly, there are those countries that are keen to make biotechnological advances on their own and are concerned that human genetic sequences be regarded as *pre competitive information*. In this concern they find support from critics of the patent system in the developed world. Secondly, there are peoples within developing countries and some governments who oppose the patenting of human genetic material on moral grounds. Such opponents believe *inter alia* that patenting goes against inherent human dignity and commodifies 'life'. A third response to the patenting of human genetic material taken from developing countries has been the exercise of tighter control over all international collaborative agreements for genetic research. This is seen as necessary to protect human subjects of research as well as to form a negotiating point for any benefit sharing of commercial applications of such research.

The position of the bioindustry in the developed world on the other hand is one that relies on the incentive effect of patents, without which crucial research would never take place for lack of secure financial backing. Since information is expensive to produce but relatively cheap to copy, the argument goes, patents are indispensable to research and development in biotechnology, as elsewhere[35]. This is a claim that is

recognised in the European Biotechnology Directive[36]; Recital 2 refers to 'the considerable amount of high-risk investment' in the field of genetic engineering, research and development, which only 'adequate legal protection can make profitable'. It is also clear that the patent system can result in opportunistic behaviour that can prove socially costly. Many commentators agree that the patent system as it currently stands provides ample scope for such behaviour[37]. Given the international relevance of genetic research for global health, opportunistic behaviour in this sphere could prove inordinately costly. To prevent this, policies and responses in developing countries should be taken into the paradigm of evaluation of the pros and cons of patents in any particular technology within developed countries.

1.2 The patent system recognises and protects the genetic information in human genetic material as inventions, provided standards of patentability are fulfilled. The tangible human genetic material taken from a human source. (in this context, from a developing country) goes into an 'invention' as 'intangible' genetic information. Therefore the link between the source and the actual invention is not strictly relevant to the patent system[38]. Hence the only way to evaluate how widespread the practice of 'patenting human genetic material' from developing countries is, is through full text searches of patents. As the patentee is not obliged to describe details not relevant to the description of the invention, the full text searches are likely to lead to partial information alone. Depending on the search profile it can lead to far too many lost answers or too many non-relevant hits. As part of this study, Derwent, a leading commercial patent information service provider was approached. This author's opinion on this is shared by Derwent that such a study could only be done with necessarily imperfect fulltext searches.

Undoubtedly, this kind of information is essential for effective policy formulation. Given the increasing relevance and sensitivity of this question, patent applicants for patents comprising human genetic information should be obliged to mention the source of the genetic material. It is recommended that an indexing method for this should be developed within patent databases. It is likely that such a move can be done relatively easily, as often the information may be available in the patent already, but not accessible through conventional 'value added' patent database searches. It is therefore recommended that patent information services be encouraged to develop such an indexing method.

Although it would take considerable discussion between various parties, it is recommended that steps be taken to label the source of biological material in general and human genetic material in particular. Such a measure towards 'source labelling' is necessary in order to have any relevant discussion about controversial issues like human genetic material patents and informed consent for example. Such labelling should provide additional information on whether source of the human genetic material is a single identifiable person, a group of people, or unidentified samples collected for purposes other than the genetic research that led to the invention. This is essential to deter illegitimate appropriation of human genetic material and will discourage ignorance about the source of the material. This labelling measure will have to also allow for a margin of cases where the source is unknown and cannot be reasonably made known. This measure in the case of plant and animal germplasm, will enforce international law under the Convention of Biological Diversity and make it easier to enforce ethical standards in human genetic research[39].

There is, of course, the oft-repeated objection that the patent system should not be encumbered with such details as it was never meant to take circumstances extraneous to the invention into account. However, such a measure could well work in the favour of domestic patent systems by ensuring legal title to the human genetic invention and helping to avoid the possibility of legal actions. It would also be a positive step towards maintaining good public relations and the need to leave avenues open for future access to material for genetic research. The latter, especially is a compelling argument for such a measure. It is hoped that this report will make it evident that international, legal, ethical and political developments have made the implementation of 'source labelling' for biological material necessary.

TABLE 2

STATEMENTS BY INDIGENOUS PEOPLE WHICH HAVE REJECTED THE HUMAN GENOME DIVERSITY PROJECT INCLUDE

Karioca Declaration, Brazil, June 1992 – As Assembly of indigenous people worldwide, Spanish and English Speaking, which met before the UN Conference on Environment and Development (Earth Summit) in Rio De Janiero
The Mataatua Declaration, June 1993 – A meeting of over 150 participants from 14 UN member states, Spanish and English speaking, developed and tabled this Declaration with the UN.
The UN Working Group on Indigenous Populations, tenth session, July 1993 – Annual UN meeting attended by 300-400 indigenous representatives.
World Council of Indigenous People – WCIP renamed the HGDP, the Vampire project.
Maori Congress Indigenous Peoples Roundtable, June 1994 – Indigenous participants from the World Council of Indigenous Peoples, Greenland Home Rule Government, COICA (Peru), Treaty Six Chiefs (Alberta) and Government representatives from Vanuatu, PNG and Fiji.
Geneva IPR workshop, August 1994
Latin and South American Consultation of Indigenous Peoples Knowledge, Bolivia, September 1994.
Asian Consultation on the Protection and Conservation of Indigenous Peoples Knowledge, Malaysia, February 1995.
Indigenous Leader's Meeting about the HGDP, Arizona February 1995 – Leaders from the US, Canada, Panama, Ecuador, Peru, Bolivia and Argentina.
National Congress of American Indians, Resolution No NV 93-118.

2

PATENTING AND INFORMED CONSENT OF PARTICIPANTS IN GENETIC RESEARCH

The following question was used as a guide to this section:
Should there be prior informed consent, from the people donating genetic material, to patents being sought for that material or products derived therefrom?

2.1 The question of informed consent is extremely problematic, partly because of the different contexts in which it is used as a necessarily imperfect resolution. The answer to this question can simply be based on a proper understanding of what *informed* consent means. It would follow that not to get consent to patent an invention based on or using biological material of human origin is not to get *fully informed* consent for the obtaining of the material.

To understand the reach and rationale of the above statement, we need to identify the basis for the taking of informed consent for biological material in the first place. This issue thus raises further questions. Using the vocabulary of the original term of reference; why is informed consent necessary from people 'donating' genetic material? And does this reason hold good for possible patents on the genetic material as well? This question presumes an answer in its use of terminology. The term 'donate' assumes a conveyance of 'property' to the person the donation is made, and all the rights associated with it. In the case of a true donation the donee has every right to use the material as he wishes, even patent it (see endnote 2). It is very important to identify literature where terminology is being used in less than accurate ways and the following discussion aims to help in this.

Informed consent developed as part of an ethical process to obtain agreement with patients to proposed research in a health context after the Nuremberg trial [40]. The doctrine of informed consent is applied to both medical treatment and research. Before a person is asked to consent to any sampling or treatment they must be provided with certain information. The information must include at least the following, presented in a language the person 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 and (b) a description of the risks and benefits of the resultant information[41].

Since the origin of the doctrine, its use has been extended to many other contexts. Its popularity is based on a presumption that informed consent is an indication of the autonomy of the individual who gives it. Autonomy literally means self-rule of an individual acting as a free agent and has many aspects to it – autonomy can mean freedom from coercion, freedom to follow reason, or as the freedom to follow ones values – both whimsical and 'authentic' ones[42]. When informed consent is not taken the implication maybe that the will of the person is not expressed, and is therefore an infringement of the person's autonomy. However, as a process, informed consent is indeterminate and is given form by the imperatives of the particular situation it is used in. Its efficacy depends wholly on the substantial equality of the person conveying the information and the person receiving it. The source of the genetic material in a therapeutic or a non-therapeutic context has only the information being conveyed to

her to rely on, and this has to be done in a manner in which she understands it. This process is made more difficult when the two parties are from different cultures, where things are understood in very different ways. For example, some guidelines insist on written consent from participants in research[43]. Such a stipulation may be meaningless for people in a different culture where premium is laid on other forms of communication. The Human Genome Diversity Project's (HGDP) Model Ethical Protocol for Collecting DNA Samples acknowledges this; 'The informed consent process, even in the best of situations, with the most technically sophisticated audiences is rarely perfect'[44].

Therefore, it is submitted that informed consent should not be equated with full autonomy and respect for the human being. It can be useful in some contexts; these contexts are limited, and real autonomy cannot be reflected by informed consent alone. The limitations of informed consent is necessarily exacerbated in the context of research on peoples from developing countries where poverty of participants is far more likely to be a significant circumstance, especially if the research is conducted by people perceived to be 'wealthy outsiders'. Indeed, informed consent has been denounced by indigenous peoples' declarations as being antithetical to their values[45]. It is not possible to list all the situations where informed consent is more effective than others, but the aim of this discussion is to highlight the limitations of informed consent. The doctrine should be used at best, as an indication of lack of intent to coerce on the part of the '*first knowing appropriator*'[46], and has value in being a universal *least* common denominator for participation in research.

Informed consent has come into international focus now with respect to the Convention on Biological Diversity (CBD). The convention has led to a number of local legislations in developing countries that *inter alia,* enforce a requirement of prior informed consent for taking of genetic resources from the national governments as well as local level populations[47]. Any possibility that the CBD could be interpreted to include human genes as 'genetic resources' within the meaning of the Convention was eliminated at the Second Conference of the parties in November 1995[48]. Therefore, there is no international consensus on the mechanics of informed consent for human genetic studies, although various developments in this context may be taken as an indication of an international agreement as to the need for informed consent at the *very least,* for research on human subjects. In the context of population studies, for example, UNESCO's International Bioethics Committee, recognised that 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'[49].

The regime with respect to the need for informed consent is distributed over various international regulations and ethical principles with widely differing enforceability. It would be in the interests of certainty of the law to accept informed consent as a legally binding principle in the case of human genetic research as it is in the case of other genetic resources under the CBD. Such a measure will provide impetus to national governments to take steps to ensure compliance with what some

commentators have referred to as a human right (see discussion under Section 5 below).

2.2 There are two possible reasons why the process of informing the source should include discussion of the possibility of patents being taken out on the genetic material. Firstly, because the autonomy of the source may be affected by any subsequent commercialisation via the patent system of which he is unaware and has not had a chance to explicitly dissent from. Secondly, the presumption may be that informed consent is required from the source that 'owns' his own tissue and therefore should consent to its use in a commercial context. Here 'informed consent' is made to function as an instrument of conveyance of property, which further obfuscates the nature of the process. The language used by some of the informed consent mechanisms like 'abandonment' or 'gift' adds to the impression of 'conveyance'.

The central problem in both of these situations is the relationship between the source and the human genetic material taken from her. One position that has been presented in the literature is that people should have full ownership rights in their body and their separated bodily parts. This is a problematic position to take[50], because it gives too much away. It has been argued that if a person has full property interest in her own body then she must be allowed among other things to sell those parts to the highest bidder in the market. Most legal systems do not permit this. On the contrary, a strong presumption all legal systems is that human beings cannot be owned. To be owned is generally accepted as being offensive to human dignity. This same reason extends to not allowing the person herself to indulge in behaviour offensive to human dignity, albeit with her own body. Thus internationally, the 'sale' of organs is illegal, and the stipulation that 'no direct financial gain should accrue from the human body'[51] is a well established one. Therefore, full self-ownership is not a position of choice for many policy reasons[52].

BOX 2

To talk about the relationship between a person and her body in a coherent way, certain common principles must be acceptable. The following discussion will not be applicable to those legal systems that do not conform to the following broad principles.

1) No person should have the right to sell the human body in whole or in parts.
2) Every person has the freedom to 'use' her body in any way she wishes to.
3) The right to bodily integrity is a part of this freedom to use her body, and is a well-protected right.

The starting point for a discussion of the relationship between a person and her body is often the freedom she enjoys to 'use' her body. Sources of human genetic material have the freedom to use their body as they wish, subject to the law, which, in most liberal democracies would put a high premium on the degree of this freedom. The source of human genetic material also has a right to bodily integrity. From this follows that the source has a right to control how her separated bodily parts are used as long as any use may potentially offend her privacy or dignity. This right to insist that others do not meddle or interfere with separated bodily parts does not oblige legal

systems which recognise the right to bodily integrity to enact new rules. The existing protection for the body and her personal security prohibits the interfering with whole bodies and is a right to keep bodily integrity intact. From this flows her right to control how separated bodily parts are used.

But this right is rarely a *full property* interest; it is an ownership interest that is short of full property interest[53]. To say that this interest is full property goes too far because she would then be able to convey ownership to another and this other should then be able to receive the property right in her separated bodily parts. However, if we agree that the bodily freedom is the basis, it may be argued that nothing in this principle alone gives a person the right to sell his separated bodily parts to whomsoever he wishes. The mere fact of separation from the whole body cannot create full ownership rights.

But the ownership interest that the source does have is protected, *inter alia*, by a procedure that explains what may reasonably be expected to happen to her separated body tissue. Commercialisation of human genetic material has the potential to be very important to many people, and hence it may be argued that the process of 'informing' the source would be incomplete without such information. A reading of various regulations show that what is being protected in such a process is this 'ownership interest' without going so far as to give people self ownership in their bodies. On the other hand, a number of statements and declarations have claimed self-ownership of bodies as a means of empowerment of sources of genetic material[54]. The language should be evaluated for what it exactly means, for often property rhetoric is used to bolster the right of people to know and control the different uses to which their bodily tissue is put. Thus, whether it is viewed from an autonomy (personal rights) perspective or a ownership perspective, the process of informed consent seems to require that information provided to the source include the possibility of her human genetic material being patented, if this is one of the potential results of the research.

The most common framework of control over human tissue in developing countries is the model of a public repository from which consent is to be taken for all collaborative projects and for the commercial use of any human genetic information that arises out of such research. Guidelines from developing countries lay emphasis on individual informed consent as well community consent where relevant. An interesting question that arises given the presence of national authorities from whom relevant authorisation must be taken (For example in India and China) is whether this amounts to making human tissue 'state property' in these countries. Many of these regulations also specify mechanisms by which any benefits that result out of the research are to be channelled to the people participating in such studies.

BOX 3

India and China provide an example of state directed utilisation of human genetic resources. The regulatory provisions in both these countries make it clear that self-ownership of human tissue is not a matter of concern as much as national ownership of genetic resources.

India: Ethical policies on the human genome, genetic research and services was drafted by the National Bioethics Committee which was formulated so as to be in keeping with the 'Ethical Guidelines for Biomedical Research, 2000' Developed by the Indian Council of Medical Research. The policy states that 'International law allows for the identification of ownership of sovereign rights over human genetic material (like anyother biodiversity, plants, animals, microbes) which shall be implemented'.

China: In June 10, 1998, Interim measures for the Administration of Human Genetic Resources issued by the state council of China came into force. The measures were enacted for the purpose of 'protecting and rationally utilising human genetic resources in the People's Republic of China, strengthening the research and development of human genes and benefits'. According to article 4 of the Measures, the state adopts a reporting and registration system on important 'pedigrees' and genetic resources in specified regions. Further, No institution or individual may sample, collect, trade, export human genetic resources or take them outside the territory of the People's Republic of China, or provide then to other countries in any form without permission (See table 4 below).

The mechanics of informed consent as mentioned before, has to be tailored to meet the requirements of particular situations. In the context of human genetic material, this is a complex task. For example there may be circumstances where an individual is unable to give consent. In such cases it has to be decided whether proxy consent is acceptable for the commercialisation of research. The Human Genome Diversity Project plans to use stored tissue samples both newly collected and previously saved. In the case of the latter, the samples may be anonymous or may have been collected for different purposes. Thus the use of tissue samples originally taken for a reason different from the genetic research with potential commercial applications is another special case.[55] Another example of circumstances in which informed consent is significant is in the use of human body parts discarded after evasive medical procedures[56]. Informed consent procedures are not easy to implement given the variety of sources of genetic tissue, but on a fundamental level there is strong support for the position that the process must include discussion of the possible commercialisation of the results of the study.

2.3 There is another important reason why prior information should be given to sources about patents being sought on the genetic material or products derived therefrom. Many commentators regard genetic material as a special case because of the deeply personal nature of the information that it provides about the person as well as about her family or other people sharing her genetic characteristic[57]. This strengthens the position that every person must have an opportunity to deny the possibility of patents on genetic material taken from her or products derived therefrom. In effect this argument is part of the autonomy debate, but the sensitive nature of it requires that special attention be drawn to it. Similarly, there is a possibility that participants in research may hold views that patenting of human genetic material is antithetical to their spirituality and culture. Opinions of the following sort are not uncommon; 'We oppose the patenting of all natural genetic

materials. We hold that these cannot be bought, owned, sold, discovered or patented, even in its smallest form'[58]. Therefore, there is reason to think that participants in a genetic study should be given the benefit of doubt and a chance to express their wishes with respect to patents on their material.

The real problem is that for the patent system, the material taken from the source is seen to be 'legally and factually' distinct from the information that goes into the patent[59]. The dichotomy between human (genetic) material as a physical tangible entity and the 'genetic invention' as an intangible entity with different aspects of ownership and control appears to disempower the source of the material. Many commentators who oppose patents on human genetic material draw arguments from dignity of human life to oppose this reductionism inherent in the patent system[60]. The gene for some people represents a metaphor for personhood and identity.[61] If autonomy of individuals is an important guide to action in law and ethics, then it follows that sources of human genetic material should have a chance to dissent from commercial manipulation of their genetic material. On the basis of this discussion, it appears that, in all circumstances prior informed consent from the source of human genetic material must include information about any patents that may be sought for that material or products derived therefrom.

3

THE RELEVANCE OF COMMUNITY CONSULTATION AND CONSENT

The following question was used as a guide to this section:
Is it sufficient to obtain the consent of the person donating the genetic material or should consent be obtained from others sharing characteristics of the material?

3.1 As the discussion under section 1 makes clear, scientists have reason to focus on communities for biomedical research into the genetic determinants of common diseases[62]. The genetic information that results from such studies may have repercussions for all in the community who share the genetic characteristics. For example, Ashkenazi Jews who participated in a study on cancer have expressed concerns that they may become targets for discrimination[63]. Because genetic information is of a special nature, some research guidelines specify circumstances in which community consent should be taken. For example, this is discussed extensively in the HGDP's draft Model Ethical Protocol for Collecting DNA Samples[64], Guidelines for research involving aboriginal communities, exemplified by those of the Australian National Health and Medical research Council[65] and the guidelines proposed by the Indian Health Service, designed as a concise working document for multiple groups, including American Indian and Alaska Native communities and People[66].

Taking group consent is dependent on what the characteristics of the group are; how cohesive the group is; whether they have a political authority or other representation etc. The term community delineates a wide variety of human associations, from tribes to municipalities to religious adherents. No single set of characteristics or consent regulations will fit all types of communities. Charcteristics of particular importance or relevance to communities in biomedical research can be identified and used to delineate seven types of communities. These are described in Table 2 below[67]. The table shows that the nature of communities may be too diverse to make any generalisations about the mechanisms of group consent.

The most important question in this issue is under what circumstance does involvement of the group sharing genetic characteristics become relevant? The answer to this question can be derived from the nature of the genetic study itself. If the aim is to study the genetic condition expressed in a certain population or if tissue samples are required from a large number of people belonging to a particular community, then the consent of the group may become relevant. This is because *inter alia,* the information that results from such a study may have direct relevance to the health of the community, or the patenting of genetic material may go against their spiritual values, or the group may want to negotiate certain benefits for their participation in the research. Genetic data that can be associated with an identifiable person and stored or processed for research or any other purpose, according to International guidelines, has to be held under confidentiality[68]. Similar issues of privacy and confidentiality arise when a community is involved, and hence it may be argued that informed consent is a pre-requisite to community self determination just as it is for individual autonomy.

BOX 4

A consultation document of the European Society of Human Genetics, which is a draft valid until the 8th of Oct 2001 has this to say about group consent in the context of population studies and DNA storage and banking for biomedical research:
Para 15- If a population is to be the subject of research, additional consent may be required at a group level through its culturally appropriate authorities. The precise form of the consent must take cultural differences into account and respect minority rights.
Para 16- If the sampling is done by a group from a different country, regulations from both the country of origin of the samples and the country of origin of the researchers should be respected in order to maximise the protection of the rights of the sampled population.

The proposed Model Ethical Protocol for Collecting DNA Samples of the HGDP deals expressly with ethical and legal issues that are raised when a project seeks DNA explicitly from populations. The Guidelines on group consent say the following –
'In addition to individual informed consent, the Committee believes that a further consent process is required. The HGDP intends to study populations, not individuals. As a result we believe that both the populations and the individuals must give their free consent to participate. This is particularly true because the effort to include samples from throughout the human species means that many of the populations sampled will not be a part of the industrialised world, where genetic studies to date have concentrated. Many of the populations that might participate in the HGDP are politically or economically marginal in their countries. They have faced discrimination, oppression, and even genocide. Under such circumstances it cannot be ethically appropriate to sample some members of a group when the group itself has not agreed to participate in the HGDP. Such methods would themselves be an attack on the autonomy of the population.

TABLE 3

CHARACTERISTICS OF TYPES OF COMMUNITIES

Type of community →

Community Characteristic	**Aboriginal** e.g. Kahnakawe	**Geographic/ Political** e.g. Iceland Group	**Religious** e.g. Amish	**Disease** e.g. HIV	**Ethnic/ Racial** e.g. Ashkenazim	**Occupational** e.g. nurses	**Virtual** e.g. e-mail discussion group
Common Culture and traditions, cannon of knowledge, and shared history	++	+	++	+/-	+	++	+
Comprehensiveness of culture	++	+/-	++	-	+	+/-	-
Health-related common culture	++	+	++	++	+	+/-	-
Legitimate political authority	++	++	+/-	-	-	+/-	-
Representative group/ individuals	++	++	++	+	+	+/-	+/-
Mechanism for priority setting in health care	+	+	+/-	+	+/-	+/-	-
Geographic localisation	+	++	+/-	+/-	+/-	-	-
Common economy/ shared resources	++	++	+/-	+/-	+/-	-	-
Communication network	++	+	+	+/-	+/-	+	++
Self-identification as community	++	++	++	+/-	+	+/-	+

++ The community nearly always or always possesses the characteristic
+ The community often possesses the characteristic
+/- The community occasionally or rarely possesses the characteristic
- The community very rarely or never possesses the characteristic

3.2 Clearly, the application of the ethical principle of informed consent and respect for integrity is a more complex process at the level of populations. The lines between genetic testing of individuals and population genetics may not always be clearly demarcated. Careful consideration is called for in order to ensure that collectives who are potential sources of genetic material understand the goals of the research, risks involved, use to which the research could be put as well as the rights of individuals and the group involved. If the community agrees to take part in a genetic study, individual autonomy means that no member of the community can be forced to take part in it. On the other hand once a community has declined to participate in a study, the ethicality of approaching individuals in the community is questionable. Therefore group or community consent is dependent on the nature of the relationship between the individuals within the community and the community itself. In some research guidelines, 'culturally appropriate authorities' are specified, and sometimes state government authorisation is required in addition to community consent.

In the case of the regulations drafted by the Indian National Bioethics Commission[69] when research pertains to a specific community (e.g., an ethnic group, an organisation of patients), it states that it is desirable to obtain group consent before obtaining individual consent. Group consent must also be documented. It recommends that agreements for sharing of benefits arising out of the research (such as, intellectual property rights, access to products or procedures, capacity building) be established before commencement of a research study.

Potential community protections extend from genesis of the research to publication of the results. The following maybe taken as a rough guide to the different stages of informed consent and community consultation that is commonly envisaged[70].

- **Consultation in protocol development**: The researcher must show respect for the community's culture, seek community input, ensure research is useful to the community, and respect the community's knowledge and experience.
- **Information disclosure and informed consent**: Disclosure to the community should be non-technical, and appropriate face to face meetings are encouraged. Adequate time for review should be given, and community consent is required for further protocol changes.
- **Involvement in research conduct**: Skill and research expertise should be transferred to the community, the community should be reimbursed for research costs and kept informed about progress.
- **Access to data and samples**: The researcher must seek community consent for further use of samples, and storage of data should be negotiated.
- **Dissemination and publication of results**: The researcher must seek consent to identify the community, involve them in manuscript preparation, take their consent for publication and provide a final report to the community.

Detailed legislation with respect to access to genetic resources including proposed human genetic studies exist in many developing countries. For example, legislation on Philippines, Costa Rica and the Andean Community recognise the rights of indigenous and local communities to decide on access to resources on their territories and lands. The Andean decision no: 391 and the Biodiversity Law of Costa Rica provide that information concerning the origin of the genetic resource in question and proof of prior informed consent of government authorities and holders of traditional knowledge are to be provided in patent applications. Also, decision 486 of the Andean

community relating to the patenting of traditional knowledge of indigenous and local communities provide for *nulidad absoluta* of a patent, in cases where prior informed consent of indigenous and local communities was not granted regarding the products or processes to be patented.

There are developing countries where such legislation does not exist or has not been made widely known. Some of these regulations may be administrative rulings or memoranda and therefore harder to locate. It is suggested that such regulations should be compiled and made known to researchers through bodies like the Medical Research Councils. This would help to bring down uncertainty in the research community as to what exactly may be done and what may not be.

BOX 5

In India an Indo-Foreign Cell (IFC) was set up in the Indian Council of Medical Research (ICMR) in the early 1980s to co-ordinate collaboration in biomedical research between India and other countries/ international agencies. Also, biomedical research has figured in almost every bilateral agreement in the field of Science and Technology in addition to a few specific agreements signed by the Ministry of Health and Family Welfare with other countries as well as those signed directly by the ICMR[71].

Guidelines with respect to transfer of human biological material for biomedical research were issued in 1997[72]. This states that, 'in order to protect the rights of the Indian study subjects as well as Indian scientists/organisations, Memoranda of Understanding and/or Agreements on Material Transfer should be entered into between the collaborating partners (Indian and Foreign). These should, according to the requirements of case under consideration, include items pertaining to identification of the collaborating or sending/receiving parties, background, the material to be transferred and its quantities, purpose of transfer, the research to be carried out using the material, confidentiality, intellectual property rights, filing of patents, arrangements for future commercial exploitation, reporting, publication rights, indemnification, termination of agreement, assignation or transfer of agreement/rights, safety norms to be observed, shipping arrangements, qualified user information, and any other matter that may be relevant to the particular exchange of material.

The increased awareness about biomedical studies in the aftermath of the launch of the Human Genome Diversity Project, has also meant that some communities and states have chosen to enter into sophisticated contracts with researchers directly as to how tissue samples may be collected and what use can be made of it. For example, the small Pacific Nation of Tonga recently contracted with the Australian Biotechnology company, Autogen to carry out genetic studies. Tonga provides a well-characterised self contained and stable ethnic population over many generations.[73] The Tongan Ministry of Health is expected to identify families with high incidence of certain diseases particular to the region such as early onset diabetes and obesity. In this context, the Autogen ethics policy states with respect to collectives participating in the research, that 'their welfare, rights, beliefs, perceptions, customs and cultural heritage will be respected'. Although the Tongan government will own the stored tissue, The Tongan people will be given free access to any drugs that are developed from the research and the country will receive benefits from royalties or profits arising from the new drugs[74]. Similar projects in Iceland and Estonia have statutory backing. In Iceland, people have to specifically *opt out* if they do not want to participate[75]. Here, the fact that the Icelandic Parliament approved the scheme may imply *political*

consent; but this variation of 'community informed consent' remains controversial. In Estonia, however, the Human Genes Research Act, enacted in Dec 2000, allows individuals to *opt in*[76].

Ultimately, the operation of community consent is dependent on the characteristics of the community. A few of the factors that are important to determine how particular protections are functionalised are health-related common culture, legitimate political authority, representative group or individuals, common economy or shared resources, self identification as a community etc. The protection for a community will be maximised if researchers from a different country were to respect protections in their country of origin as well as the regulations in the country of origin of the genetic material. Here it is recommended that efforts should be made to institutionalise the links between ethical regulations and commercialisation. Currently it appears as though the two exist in parallel creating a false dichotomy. If there is an international consensus that community consent for research on the community is necessary then it may be argued that community consent for commercialisation is also essential.

4

BENEFIT SHARING WITH THE RESEARCH PARTICIPANT.

The following question was used as a guide to this section:
What provisions should there be to ensure that donors of the original material or a group to which they belong share in any of the benefits arising from any patents on that material or product derived therefrom?

4.1 This issue raises the question of the circumstances under which people who give genetic material for research are entitled to share in the benefits of such research, and what the nature of such benefits should be. At first look, promising a share of the benefits to a potential participant in a genetic study seems to contravene ethical principles that specify that the body or human genome in its natural state should not give rise to financial gain. Also the ethical validity of the informed consent that is given under the promise of a share in benefits to be gained becomes questionable.

This seems to be reflected in for example, the Opinion of the European Group on Bioethics given on 21 July 1998 to the European Commission. The opinion says that all member states of the European Union adhere to the principle that 'donation' of human tissues must be free, following the example of blood, and that this rules out any payment to the 'donor', except for remuneration for constraints associated with tissue removal. The opinion acknowledges that there are views that for the 'sake of fairness, when the tissues become even indirectly a source of profit, donors should be paid'. But the opinion goes on to say that, so far, arguments in favour of the altruistic nature of tissue donation have prevailed and this arises out of the desire to avoid all risk of exploitation or the perception of a human being as an object[77].

Some critics propose this 'gift' model for human tissue samples as the best option. This avoids the ethical tangle of 'commodifying' human genetic material, and is a partial acceptance of the property model and is therefore seen to be empowering the participant who is given the choice of making a 'gift' towards the progress of science. However it has also been suggested that the gift model does not exclude possibility of forms of benefit sharing while retaining the rhetoric value of the participation of a source in a genetic study[78]. One leading commentator recognises that while tissues are no longer to be considered abandoned or waste, given their potential for genetic information, promises of eventual financial rewards to sources cannot be the answer. 'If DNA is neither "person" nor "thing" but rather requires a *sui generis* approach, it may be more respectful of its unique status and qualities to consider its use in genetic research as a gift – a gift conditional on the individual choices made[79]. The advantages of such an approach is that the control of the source is maintained within the property vocabulary, and the *conditional* nature of the gift means that benefit sharing can still be negotiated.

To give another example of a gratuitous approach, the Fundamental Principles of Research on the Human Genome drafted by the Bioethics committee of the Japanese Council for Science and Technology in June 2000, states in Principle 17 that 'all research samples should be provided gratuitously'. Part 2 of Principle 7 also says that in the event that an outcome obtained as a consequence of a research project becomes the subject of intellectual property rights or other rights, these property rights are not

attributed to the participant[80]. However, the provision of benefits to the participating community in connection with the collection of samples is an important part of ethical research design under the HGDP's proposed model protocol[81]. Appropriate return for an individual's participation and avoidance of inappropriate 'bribery' is far more complicated than appropriate return in the context of a community. The HGDP protocol adopts broad concepts of honest, legality and appropriateness – of nature, scale and distribution as guiding principles.

The line between unethical inducement and appropriate benefit sharing is a fine one. The sophistication this calls for should not be an obstacle to the development of appropriate benefit sharing mechanisms, especially where developing countries are concerned. In contrast to the gratuitous approaches described above, many developing countries in their guidelines for participation in human genetic research specify the importance of benefit sharing, at a level beyond the individual. This takes the form of medical benefits to a participating community, free access to any resulting drugs, technology transfer to the people, etc. For example, the Indian National Bioethics Commission Policy recommends that it should be obligatory for national/international profit making entities to dedicate a percentage (e.g., 1% - 3%) of their annual net profit arising out of the knowledge derived by use of the human genetic material, for the benefits of the community. Many developing countries make such benefit-sharing conditional to authorisation of human genetic research. There are two advantages of such benefit sharing on a national or regional level. Individual participants cannot be enticed into any research with the promise of personal gain, but collective benefit may play a part in the decision to take part. Secondly, since the terms of such benefit sharing are contractual or statutory, national authorities have greater control over the specifics of such agreements.

The guidelines in developing countries are usually in the form of ethical principles, or administrative regulations under which international research collaboration is approved. Only some of them are legal requirements (For example, legislation of the Andean community, (see Table 4 below). Therefore their enforcement is largely dependent on the integrity of researchers and in cases where the country of origin of the researchers is different to where the genetic material is being collected, the oversight of compliance is difficult. To have real effect, such regulations should be backed by equivalent regulations in the country of origin of the researcher, which encourages her to comply with overseas regulations as well.

While it appears that direct financial reward to a source in exchange for genetic material falls foul of ethical principles, it does not prevent indirect benefits. The Human Genome Organisation's statement on the Principled Conduct of Genetics Research exemplifies this when it prohibits *undue inducement* through compensation for individual participants, families and populations. However it goes on to say that this prohibition, does not include agreements with individuals, families, groups, communities or populations that foresee technology transfer, local training, joint ventures, provision of health care or of information infrastructures, reimbursement of costs, or the possible use of a percentage of royalties for humanitarian purposes[82].

The particular benefit that may be accorded depends on the ability of the source to make use of it. For example technology transfer will not be useful to a community which does not have trained personnel, and medical benefits require basic

infrastructure. Thus the guidelines produced for researchers of the HGDP proposed among other things that the 'transfer of technology to the developing regions of the world, should contribute positively to the development of self-sufficiency in these regions. The help given should not be superficial or of only short term usefulness'.

Internationally, there is some recognition that benefit of advances in understanding the human genome should be made available to all. A key characteristic of biotechnology industry is its highly internationalised and interactive nature.[83] The UNESCO Declaration on the Human Genome and Human Rights devotes a number of provisions to urging states to make every effort to foster scientific and cultural co-operation between industrialised and developing countries in the international dissemination of scientific knowledge concerning the human genome, human diversity and genetic research. Article 19 is of special significance in so far as it lists out a framework for such co-operation. Thus states should seek to encourage measures enabling (para 3 of Art 19):

'developing countries to benefit from the achievements of scientific and technological research so that their use in favour of economic and social progress can be of benefit to all'.

There are a number of international law and policy guidelines that emphasis the importance of technology transfer. Article 7 of the TRIPS agreement represents a grand bargain between stronger intellectual property rights that contribute to the promotion of technological innovation and transfer and dissemination of technology. With the growing technological gap between developed and developing countries, the developing countries would like to see greater mechanisms that promote technology transfer[84]. India for example, has called for the establishment of a Working Group on technological Transfer under the WTO[85]. Therefore, this coupled with the provisions of the UNESCO declaration on the human genome, provide considerable support for technology transfer as a means of benefit sharing in the case of human genetic studies.

The case of medical care or drugs as part of the benefit sharing agreement is particularly apt, since genetic studies are usually done in a biomedical context and are likely to result in significant health information about the participants. For example, in the well publicised case of Carol Jenkins and the patent on a cell line derived from the Hagahai, she writes that 'the ethical obligation to intervene with medical aid was immediately obvious to the researchers'[86] As mentioned before in the Tongan case, the company, Autogen is expected to build a new research laboratory next to the hospital in Tonga and provide modern equipment for the hospital and annual research funding for the ministry of health, apart from free access to any drugs that are being are developed from the research.

Provisions that specify a share in intellectual property rights are usually to be found in the regulations of the more advanced developed countries that have their own genetic research programmes under way. These countries include India, China and Brazil. In one proposal from India it was proposed that in collaborative research, a 'majority share' of intellectual property rights should be held by the collaborating Indian site and 20% of the benefits accruing from such a patent being used by the individual institutions to develop better services for the population that provided that material[87]. Chinese regulations also have clauses that provide for the equitable sharing of

intellectual property rights in the case of collaborative research, with profits from resultant patents to be shared in proportion to the contribution of the two bodies concerned[88].

Research institutions and private bodies based in the developed world that aim to conduct such research should be made aware of such regulations and encouraged to actively follow the principle of benefit sharing. Many of these regulations are conditional on providing access for research, and should be on mutually agreeable terms of the internationally collaborating sites, as well as wishes of the participating groups. At the least, all laws and regulations within the site of collection for genetic samples must be respected. Further, given the provisions of the UNESCO Declaration, the possibility of benefit sharing through dissemination of medical benefits or technology transfer or even assigning a percentage of profits internationally for developing country interests should be considered.

BOX 6

THE ORGANISATION OF AFRICAN UNITY

The group of 53 African states has adopted a model law which aims to be an alternative to a generalised approach in intellectual property law to biotechnology. This framework law follows commitments undertaken in the TRIPS agreement, with a view to combating the exploitation of African countries' genetic resources by more developed countries. Developed by the Science, Technology and Research Committee of OAU, it endorses a number of the fundamental principles of the Convention on Biological Diversity; state sovereignty over resources, need for prior consent on the part of those populations concerned, and equitable sharing of benefits derived from the commercial utilisation of such resources. Although the law does not explicitly focus on the human genome, the model is based on community rights and access to biological resources. The following are specified as conditions of access:

- Prior informed consent of both the State and the indigenous and local communities.
- Issuance of written authorisation by relevant national authorities.
- Determination by these same authorities of the amount of fees payable for the authorisation to exploit, fees being determined on the basis of sales of exploited resources.
- Implementation of mechanisms to ensure the fair and equitable sharing of benefits deriving from the commercial utilisation of such resources, in particular through the payment of fees levied into a special fund for the financing of projects defined by local communities with a view to the sustainable development, conservation, and use of genetic resources.

5

PATENT LAWS IN DEVELOPED COUNTRIES WITH RESPECT TO INFORMED CONSENT AND BENEFIT SHARING

The following question was used as a guide to this section:
Should the patent laws in developed countries play a role in enforcing any requirements relating to prior informed consent or benefit sharing?

5.1 It has been argued that the enforcement of informed consent and benefit sharing whilst currently done on the basis of national regulations and contractual agreements should be strengthened by international legal measures. In particular, the international character of genetic research means that researchers working in developed countries may seek genetic data from people living in developing countries where there may not be the same level of protection as applies elsewhere[89]. And the patent system being the fulcrum of the commercialisation of biological and genetic resources, it is argued, should be one of the means to do this.

On the other hand there are many critics of the move to enforce requirements relating to prior informed consent or benefits through patent laws. The bulk of the arguments flow from the reluctance to enforce morality under patent law. Some of the arguments that are used to express the unsuitability of moral evaluations in patent law, and there have been many vociferous critics[90], are not relevant in the context of informed consent as there is evidence of an international consensus that informed consent is necessary and that benefit sharing, desirable, as expressed in international declarations, international law under the Convention on Biological Diversity (albeit in a non human genetic material context), and domestic regulations in many countries as well as declarations of indigenous people. Moral positions of the kind that may be evaluated under Art 53(a) of the European Patent Convention (or the corresponding Art 6 of the Biotechnology Directive 98/44/EC) for example, are, on the contrary, much more diverse and hard to agree on internationally. Therefore it must be recognised, at the outset, that informed consent and benefit sharing are not vague ethical principles that are therefore difficult to enforce in law. If this is accepted, then, really the question is whether patent law in any country should be concerned with domestic laws and regulations in another country where such regulations govern the conduct of research and development of the invention.

In this section I will try to summarise the points of strength of each side of the argument. Although as presented above, there is ample reason to believe that 'informed consent' and 'benefit sharing' need not be restricted to 'moral' objections alone, the first section deals with propositions that are usually articulated in the context of the non patentability of inventions on the grounds of morality. This is because the common ground between the two is the belief, sometimes expressed, that patent law should be closed from considerations external to the strict criteria of patentability itself (Under the European Patent Convention, the inventions must be novel, involve an inventive step, be capable of industrial application and must not be specifically excluded)[91]. However, in a historical Anglo-American context patent law has always had statutory provisions that allowed for such 'external' evaluations[92].

Critics who would answer negatively to the above question emphasise that the patent itself does not grant the holder a right to produce the invention. Within a zone of non-interference she may commercially exploit the invention, unless for some contingent reason a restriction is placed on the right[93]. The approach that has been advocated for alleged 'immoral' inventions has been that the commercial exploitation of patents once granted can be regulated by other agencies[94]; and that it is in the interests of certainty of the law that moral evaluations not muddy the waters of patentability[95]. In saying this, critics are seeking ways to point out that it is only the *exploitation* of an invention that should be regulated and *after* the patent has been granted. Thus Stephen Crespi argues that the act of patenting itself is neither right nor wrong, but should be classed as being ethically neutral[96].

Critics who would like to see the patent system playing a role in enforcing requirements of morality, point out that the symbolism in the grant of a patent is not an insignificant one[97]. There may well be general reluctance on the part of legislators and other regulatory bodies to restrict opportunities for exploitation once a patent has already been granted. Moreover, the above argument does not follow from the wording of the morality provision in the European Patent Convention. Thus Art 53(a) says that 'if the exploitation of an invention *would* be contrary to morality, a patent shall not be granted. It would therefore appear that the wording *would be* in fact indicates that whether an invention is actually exploited or not is irrelevant. Thus if the exploitation would be contrary to morality it is sufficient to make it an unpatentable invention[98].

The exact stage at which morality in patent law becomes a valid condition is also a point of contention. One commentator (in the context of the Hormone *Relaxin*[99] case) says that even if a cell line that is the subject matter of a patent application was obtained in a dubious fashion, about which the patent Examiner was aware, *provided the information was not part of the application,* it would not be caught by the morality criterion. The moral prohibition, (even without publication), she says, cannot centre on a retrospective analysis of methods, since to sanction at this point would be redundant and outside the remit of legislation.[100] Another commentator (in the context of biotechnological inventions in general) says that 'unless we believe it is wrong to do this kind of research, or that it is wrong to publicise and exploit the results of this research, or that both of these are wrong, it is a strange kind of ethical selectivity that focuses on patenting in isolation'[101].

Although this may seem at first sight to be right, that the question of pre-patent events should not bother the examiners who have no jurisdiction to prohibit such research and development, things, as one critic points out, are not so simple. Suppose, for example that the development of an invention has involved the employment of slaves as 'guinea pigs' or such other immoral activity which is not ambiguously so[102]. To allow the patent encourages exploitation of the invention, and if it is immoral to profit from such behaviour a nation state can hardly countenance such activity through the grant of a patent[103]. The grant of a patent is a grant to property rights, and the association of legitimacy with the subject matter of the invention is inescapable.

The above discussion is indicative of the deep divisions in the literature in a European context where statutory provisions deny the patentability of inventions that go against morality and ordre public. Under US law however, there is no provision for exclusion

based on morality. The only way a patent application may be denied is, if it does not fit the technical standards of patentability. Another important point of difference with respect to US and European position is the opposition proceedings available at the European Patent Office. Within 9 months of filing, oppositions to the patent application maybe filed[104]. Such oppositions in the EPO are largely responsible for initiating robust discussion in the literature about the morality and ordre public clause. In contrast, under US law, there is no such provision before grant of a patent, and after a patent has been granted, the only process of evaluation of the patent is through infringement proceedings. Statutory interpretation, where it exists is of immense significance when it comes to the morality exclusion.

In Europe, Recital 26 of the Biotechnology Directive, far from resolve the issue has led to further divisions about the desirability/feasibility of patent laws playing a role in enforcing requirements of informed consent and benefit sharing.

Recital 26 says that:

> 'If an invention is based on biological material of human origin or if it uses such material, where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent thereto, in accordance with national law'

The controversy has centred on the legal status of the Recitals of the Biotechnology Directive. Of the 66 Amendments to the draft Directive proposed by the European Parliament, this provision was the only one not incorporated as an article. Whereas articles constitute the operative part of an EC Directive, the essential function of Recitals is interpretative[105]. In an in-depth analysis of the effect of Recital 26, Beyleveld suggests on the strength of legal precedent, that Recitals of the Directive are legally binding if there are no other considerations to take into account that could countermand them[106].

Prof. Beyleveld makes a very strong case for implementation of Art 26 in national law. It bears reproducing here, as an argument that leaves little scope for dissent in most cases where there is a statutory clause for exclusion from patentability on grounds of immorality. If we consider that

(1) It is a fundamental requirement of morality (in EU States) that free and informed consent must be given for the *obtaining* of biological material.
(2) Not to get consent to patent an invention based on or using biological material of human origin is not to get fully informed consent for the *obtaining* of the material.
(3) Therefore, it is a fundamental violation of morality (in EU States) not to get free and informed consent for the patenting of inventions developed from or using biological material of human origin.
(4) Therefore,
    - Even if Recital 26 did not form part of the Preamble to the EC Directive, the Recital condition should be imposed by patent offices.
    - And not to get consent patenting in accordance with Recital 26 is to violate Article 6(1) of the Biotechnology Directive.

In Europe, requirements of informed consent and benefit sharing post Directive have proved controversial. The Belgian Consultative Committee on Bioethics has stressed

that there is a need to guarantee the principle of voluntary informed consent[107]. Netherland's Appeal at the ECJ, supported by Italy and Norway, (and the Council of Europe[108]) against the Biotechnology Directive was *inter alia,* on the ground that the Directive is incompatible with the Convention on Biological Diversity, which only authorises the use of genetic resources when the peoples' concerned have given their informed consent. Although, not primarily concerned with human genetic material, the Appeal is nevertheless significant as an indication that governments in developed countries may be open to implementing requirements of informed consent and benefit sharing through patent laws.

In countries where no such morality exclusions exist, it is much harder to make a case to this effect. But even in such circumstances, reason to take note of informed consent arises because it may be argued, generally, on the basis of numerous international declarations and the existence of domestic legislation in many countries; and specifically on the basis of Art 5 (b) of the UNESCO Declaration on the Human Genome and Human Rights and Art 5 of the European Convention on Human Rights and Biomedicine and all the other legal and ethical regulations in a domestic jurisdictions, that informed consent should now be regarded as a norm in international human rights law. To recognise human rights law is to recognise that individuals have human rights from which the state itself cannot derogate. No person or body can then be granted authority to do anything that violates that right. Therefore no state, it is argued, can license a patent office to act in violation of human rights commitments[109]. Relatively, the benefit-sharing norm is not yet one for which there is as wide an international consensus as there is for informed consent.

BOX 7

The European Charter on Fundamental Rights introduces a new 'right to integrity' of the person in Art 3. It says that in the In the fields of medicine and biology, the right to free and informed consent of the person concerned according to the procedures laid down by law must be respected. There is no mention of such a right in either the UN Declaration of Human Rights or the European Declaration of Human Rights. This article is clearly the result of consensus, a minimum common denominator of European positions on biomedical research. As pointed out by the President of the European Group on Ethics, Ms Lenoir, 'Biotechnology and genetics will be the real challenge for human rights in this new century. The Charter constitutes an indication of European priorities in this area.' The links between this new provision and patent laws should be explored.

5.2 Another significant opposition to patent law taking note of informed consent and benefit sharing, is the question of enforcement of such a requirement. In a European context, industry, patent agents and patent officials who are strongly opposed to the Recital 26 condition limiting what may be patented, are specifically concerned that the condition will be difficult to manage.

As mentioned before, informed consent is not a vague ethical principle. The instances where informed consent is being embedded in regulation and guidelines is increasing at a rapid rate. Given this, the manner of enforcing it in patent law may best be done

through a certificate of compliance. Such a certificate of compliance will show that informed consent was taken according to the national regulations of the country in question, and where such regulations do not exist, a statement to that effect will suffice for the present. In such cases ethical standards that exist in the country of origin of the researcher must be adhered to. It is recommended that such a certificate should mention the origin of the material, the locus of the research, and mention whether any benefit sharing agreement has been entered into. Where material is anonymised or consent cannot be taken for any other valid reason, there should be margin to mention this. The most significant objection to such a measure is likely to be the increase in transaction costs for patent applicants. The additional costs of this would be relatively slight in those cases where informed consent was being taken; the information could be described in the text of the patent itself (See Box 7). And where informed consent is not being taken, it would provide a deterrent to unethical behaviour.

The all-important question is, if such a certificate of compliance was shown to be invalid for some reason, what would be the repercussions of it? The severest repercussion would of course be revocation of the patent, but other options like levy of penalties could be explored. There is also the question that the patent office maybe incapable of investigating allegations of invalidity of certificates of compliance. It is possible that some sort of liaison could be established between bodies like Medical Research Council in developing and developed countries who have the capacity to evaluate conditions like informed consent. This is an issue that should be studied further.

There is another option, with respect to benefit sharing which arises from a recommendation by the HUGO Ethics Committee of April 9 2000[110]. The committee recommended that profit making entities dedicate a percentage (example 1% - 3%) of their annual net profit to healthcare infrastructure and/or to humanitarian efforts. (This is reflected by Indian provisions.) This recommendation could be implemented through successful patent applications, by the levy of a fee that would go towards aspects of benefit sharing at the origin of the human genetic material.

Such measures, if left to national initiatives has potential to vary widely. International measures in this context would be in the interests of transparency so that researchers, patent offices and the courts are clear about what is required of them. Moreover failure to implement such requirements in patent law may have unfortunate implications. As one commentator points out[111] it could, firstly, lead to increased legal costs if title to patents is in some way open to question by the source of the human genetic material whose consent to the patent was not taken. Secondly, the alternative to an international consensus is to leave the question open to clauses in individual contracts or the requirements of particular bodies like local ethics boards. The result would almost certainly be increased costs in keeping track of specific requirements and general uncertainty. Thirdly, from the perspective of the bioindustry, moves towards non implementation of requirements could well be self defeating, as cases of lack of informed consent or ignoring benefit sharing can lead to damaging press campaigns.

There is also the question of the US patent system and its inclinations. Unlike the debate on Recital 26 in a European context, there is no reason to think that the US

Patent and Trademark Office is open to the idea of implementing requirements of informed consent or benefit sharing in any form. Therefore, it may be argued that in those countries where requirements of informed consent or benefit sharing are implemented through patent laws, the bioindustry may suffer a competitive disadvantage. The US response to a question posed by WIPO with respect to informed consent is revealing in that it was stated that informed consent of the source of the material has no relationship to the invention as she does not contribute to the process of arriving at the invention. At most the source may be collaterally related to a given invention, the invention itself is unaffected. (See table 4). Therefore, arriving at an international consensus over informed consent and benefit sharing in patent laws may prove to be difficult.

BOX 8

RESULTS OF SAMPLE EMPIRICAL INVESTIGATION

A search of full text patents show that some patents do mention informed consent taken from research participants, and the location of the research subjects is described. This sample study was done at the DNA Patent Database (DPD), available at www.genomic.org (last visited on 19th Dec). Patents included in the DPD are those issued in the USPTO and identified by virtue of their PTO classification and the presence of key words such as 'DNA' within the body of the patent[112]. The intent of this database, as stated on the site 'is to provide information on some of the most fundamental policy questions relating to biotechnology'. The development of such databases is highly recommended and will tremendously help demystify patents for policymakers.

Although the following data can be used as an indication of information carried in some patents, it should only be considered as partial information. Of the 20,436 patents in the database (last updated on Feb. 1st 2001), 188 patents refer to informed consent in a human context. A look at some of these 188 patents show that informed consent is described, in some more elaborately than others, in the 'Methods and Materials' section. 417 patents refer to either Asia or Africa. Again, a random look at some of these patents showed that reference to place of relevance of the invention or origin of the research was described in the section on background to the invention.

The following table 4 represents information collated from a WIPO questionnaire submitted to the Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore[113]. It consists of information provided by WIPO member states concerning practices related to the protection of biotechnological inventions. The questionnaire comprised 10 questions of which one is presented here. As far as possible, the constructed response of the countries to the question has been reproduced.

TABLE 4

QUESTION: DOES YOUR LEGISLATION INCLUDE ANY SPECIAL PROVISIONS TO ENSRE THE RECORDING OF CONTRIBUTIONS TO INVENTIONS (SUCH AS THE SOURCE OF GOVERNMENT FUNDING, THE SOURCE OF GENETIC RESOURCES THAT ORIGINATE OR ARE EMPLOYED IN BIOTECHNOLOGICAL INVENTIONS, THE GRANT OR PRIOR INFORMED CONSENT TO HAVE ACCESS TO THOSE RESOURCES ETC.?)

Country	Response	Further details
Australia	N	
Austria	N	
Bangladesh	(N)*	Currently, there is no such provision. But our country is planning to introduce legislation entitled 'Biodiversity and Community Knowledge Protection Act'.
Belarus	N	
Belgium	N	
Benin	-	
Brazil	N	There is a law pending approval, though currently not accessible.
Bulgaria	(N)*	The patent law contains no provisions of this kind and we do not plan to include any.
Cameroon	(N)*	Such provisions do not exist as yet; however, they may be developed in, more or less, the near future.
Canada	N	
China	Y*	Yes. In June 10, 1998, Interim Measures for the Administration of Human Genetic Resources issued by the state council of China came into force. The measures are enacted for the purpose of efficiently protecting and rationally utilising human genetic resources in the People's Republic of China, strengthening the research and development of human genes and promoting international co-operation and exchange on the basis of equality and mutual benefits. According to Art 4 of the Measures, the State adopts a reporting and registration system on important pedigrees and genetic resources in specified regions. No Institution or individual may sample, collect, trade, export human genetic resources or take them to other countries in any form without permission. However, these requirements are not a condition of patentability. But failure in meeting the requirements will be punished according to

		related administrative laws or regulations.
Colombia	Y*	This is according to Decision 391 of the Commission's Cartagena Agreement, which deals with Access to Genetic Resources. Not complying with such requirements is an obstacle to patentability and would justify its invalidation or revocation when the invention is obtained or developed from the genetic resources of any of the Member Countries. Decision 391 of the Commission's Cartagena Agreement, in the second additional provisions, states that, 'The member countries shall not recognise rights, including intellectual property rights, over genetic resources, derived or synthesised products and intangible components associated, obtained or developed during an access activity that does not comply with the provisions of this Decision.
Cuba	N	
Cyprus	N	
Democratic People's Rep. of Korea	N	
Denmark	Y*	Yes. The applicant must have a written assignment from the inventor, when he applies for a patent. The Order will be supplemented with a provision according to which the applicant should provide information about the geographic origin of the biological material, if he is in possession of the information. The Convention on Biodiversity must be respected. This is not a condition of patentability.
Ecuador	Y*	Yes. Enclosed is Decision 391, Common Regime for Industrial Property, from the Commission's Cartagena Agreement, current Andean Community of Nations.
El Salvador	N	
Estonia	N	
European Union	(N)*	Recital 27 of the Directive reads as follows, 'Whereas if an invention is based on biological material of the plant or animal origin or if it uses such material, the patent application should, where appropriate, include information on the geographical origin of such material, if known; whereas this is without prejudice to the processing of patent applications or the validity of rights arising from granted patents'.
Ethiopia	N*	No. We are now in the process of developing legislation on access to genetic resources, which addresses all the issues raised – such as origin, prior informed consent, etc.
Finland	N	

Germany	N	
Guatemala	N	
Hungary	(N)*	The legislation of our country does not include any special provisions to ensure recording of contributions to inventions. It is not planned in our country to introduce legislation to ensure the recording of contributions described in the question.
Iceland	N	Yes, it is planned to introduce such legislation but information but the time frame is not available.
India	N/A	
Ireland	N	No proposals at present.
Italy	N	
Japan	N	
Kazakhstan	N	
Lithuania	(N)*	Lithuanian legislation includes no special provisions. No plans for such legislation yet.
Madagascar	(N)*	Such provisions do not exist in the National legislation.
Malaysia	(N)*	Malaysian Patent Office does not have provision regarding the contributions to inventions.
Mexico	N	
Netherlands	N	
New Zealand	N	
Norway	(N)*	Our legislation does not include any provisions that ensure the recording of ownership interests to natural resources in inventions concerning biological material. There is no plan to introduce such legislation.
Panama	N	
Philippines	N*	No. Our present law on patent does not provide for special provisions, i.e. source of government funding, the grant of prior informed consent. Inclusion of such provisions in the patent law is no longer necessary because they are considered in our pending legislation for the Plant Variety Protection. (Note: the lead agency in-charge of the implementation of the PVP is the Dept. of Agriculture)
Poland	N	

Portugal	N	
Russian Federation	N*	Current legislation does not include such provisions, but this problem is now under study.
Saudi Arabia	N	
Slovakia	(N)*	Present patent legislation does not include any special provisions to ensure the recording of contributions to inventions. There are no plans for such legislation.
Slovenia	N	
Sri Lanka	N	
Sweden	(N)*	There are no such provisions as mentioned in the question and there are presently no plans in this respect.
Switzerland	N	
Thailand	N	
The Former Yugoslav Rep. of Macedonia	-	
United Kingdom	N	
United States	N*	No. The parenthetical examples appear to have no relationship to the question that has been posed. None of the examples contribute to the process of arriving at a given invention. At most, the examples may be collaterally related to a given invention; the invention, itself, is unaffected.
Uruguay	(N)*	Not currently, without prejudice to the provisions of the Convention on Biological Diversity. Nevertheless, norms relating to this issue can be found in various agreements existing in research and development organisations. A national norm is currently being studied whereby its elaboration will especially take into account Art 15 of the CBD.
Uzbekistan	N	
Venezuela	(Y)*	The Constitution of the Bolivarian Republic of Venezuela provides for the existence of information registries that involve the aspects mentioned in the questionnaire. With respect to the registry of sources of genetic resources that give rise to biotechnology inventions or are utilised in them, there exists Decision 391 of the Commission's Cartagena Agreement on the Common Regime for Access to Genetic

	Resources, which is the law for all countries that make up the Andean Community of Nations. This legal instrument encourages research projects that promote the identification; registry, characterisation, conservation and sustainable use of biodiversity and products derived from genetic resources (Art 8). In general, this legislation establishes obligations for member countries of general and specific scope for the promotion of biotechnical research, the mechanisms and forms for accessing the genetic material, as well as the registry of information related to all.
Zambia	-

Notations

( ) Indicates a constructed response
* Indicates additional information
-- No response to an applicable question
N/A Not applicable as reflected by Member States

6

POST GRANT CONTROL OVER USE OF A PATENT

The following question was used as a guide to this section:
Should the original donors of genetic material on which patents are based have any influence on how those patent rights are exploited?

6.1 The central rationale of the patent system is one of reward to the inventor for technical contributions of sufficient novelty and industrial applicability. The incentive effect this provides and its continuance is a major cause of concern for the bioindustry as the patent system, and the certainty it provides is largely responsible for the growth of the industry. Patents transpose scientific advances into technical applications especially effectively in the biotechnology sector[114]. The investment in this industry could be jeopardised if uncertain factors claim control over a granted patent. There is no precedence for post grant control as implied by the above question, within the patent system, hence it is necessary to evaluate this claim with caution.

In discussing patents based on human genetic material, we firstly, need to distinguish between patents that are being granted on the genetic material itself and patents that are granted to products and applications based on them. The distinction is a significant one in moral terms because of the 'proximity factor' in terms of identifiability of the material to a single known source[115]. This proximity is less obvious when the patent is granted on an application or product that does not entail a monopoly over all uses of the human genetic material itself.

The second significant aspect of innovations including and composed of genetic material is the combined 'physical and informational' nature. In genetic innovations, the information that is newly developed and for which a patent is granted is closely tied to the physical object which is the genetic material and cannot be communicated without this object. The significance of this duality of genetic innovations is highlighted in certain commentaries. For example, Bent *et al.* refers to DNA molecules as informational macromolecules or 'informational macromolecule invention'[116]. This duality of genetic innovations is of relevance here because it can be argued that conventional property rights, if any, over tangible biological material (from which genetic material and information can be retrieved), cannot be ignored when granting an inventor exclusive patent rights. To compare with other technological sectors, the nuts and bolts an inventor uses to make the first prototype of his invention is not directly relevant to the technical contribution for which the inventor is rewarded, whereas the same cannot be said of the genetic material the inventor in a human biotechnological context uses, because of the duality of genetic inventions in being both tangible material and intangible information, as well as due to diverse perceptions of genetic information held by people outside of the patent system[117]. Public perceptions of genetic material and information in the UK, for example, is being investigated by the Human Genetics Commission[118], and the possibility of linking the results of their consultation with the patent system should be explored.

Over and beyond the objection to patentability of human genes as naturally occurring in nature is the argument that human gene patents amount to control or ownership of 'human beings' itself. Technically, and within the patent system, this is now regarded as an inaccurate description. Many commentators have clarified that 'those of us who use the DNA in our own cells, as our ancestors have been doing for generations, should not and need not worry about patent infringement liability'[119]. In a European context similar opposition has been raised. One of the objections filed by the Green Party to the Human H2 Relaxin patent[120] at the European Patent Office, which was isolated from the tissue of a pregnant woman, was that the grant of the patent will amount to a form of modern slavery as it involves the dismemberment of women and their piecemeal sale to commercial enterprises throughout the world.

The European Patent Office Opposition Division in its decision, however, categorically stated that patents covering DNA encoding for human H2-relaxin or any other gene, do not confer on their proprietors any rights what so ever to individual human beings, no more than do patents directed to other human products such as proteins. No woman was affected in any way by that patent. Since the protein encoded by the cloned gene is produced in a technical manner from unicellular hosts containing the corresponding DNA there is no need to use human beings as the source for that protein.

This brings us to another important aspect of patents on human genetic material. The physical object of the invention usually carries the information necessary for the creation of future physical objects. Thus, the cell line that was the point of contention between John Moore and the University of California[121], was held to be 'legally and factually distinct from the cells removed from Moore's body. This case was one of the first controversial cases that caught the attention of interest groups worldwide. By disassociating Moore as the source of the genetic material, from the cell line produced using that material, this case was seen to disempower human beings whose genetic material was being used for research and possibly to create patentable applications everywhere. The dichotomy between human (genetic) material as a physical tangible entity and the 'genetic invention' as an intangible entity with different aspects of ownership and control was highlighted and to an extent established in this case. There are contrary examples as well. A recently described case presents a unique approach to balancing the concerns and rights of patients who provide biomedical research with its most significant element. This case did not involve a patent, but deals with the licensing of use of a cell line developed from a 28 year old male, whose consent for licensing and transfer was given paramount importance as also his expressed wishes as to how the material was to be used[122]. Given these above developments, many commentators who oppose patents on human genetic material draw arguments from human dignity to maintain that a person continues to have a strong interest in how human (genetic) material taken from her is used, handled and commercialised[123].

Thus extension of the sources' control over how the patent rights are exercised derives largely from an autonomy argument. Therefore, it would follow that a person (or a community) whose genetic material is patented should be allowed to exercise control over it, as their personal rights extend to the intangible property in genetic information. Such control, if recognised, could potentially cause transaction costs akin to reach through license agreement that are proving so problematic for 'research tools' in biomedical technology. However, it may be that such claims can be reduced by an

assiduous application of the informed consent doctrine. At the time of consent, the possibility of patents being granted should be explained to the source. This provides a negotiating point for the source, whether an individual or a collective, about the use of patent rights. Some developing countries like Tonga, as mentioned before, have negotiated with the relevant commercial entity about possible patents. Mutually agreed contractual terms can then be entered into. In the case of an individual, informed consent gives an opportunity to express his will about patents. In the absence of such informed consent or negotiations, the question of the claim of the source on granted patents will continue to arise and eventually be detrimental to the industry.

6.2 The second important reason why it may be argued that human sources should continue to have control over how patents granted on their material are used, is one of distributional justice. In the event of a significant discovery like isolation of a 'disease' gene, there is a likelihood of windfall of profits, given appropriate commercialisation. For example, it was reported that the rights to one gene associated with obesity were sold for $70 million[124]. In Oct this year, Nature reported that there was evidence of an 'European rebellion' against the patent on a gene for breast cancer held by US company Myriad Genetics. The patent covers BRCA 1 gene, used in tests to assess a patient's predisposition to hereditary breast and ovarian cancers. Europeans will have to pay $2400 for Myriad's screening test, whereas the French test for example, costs a third of this[125].

The possibility of windfall profits of this nature raises questions of 'unjust enrichment'. Some commentators have pointed out that the question of unjust enrichment is heightened when the source of the human genetic material, may be, for example an impoverished community in a developing country. There is an aspect of property that conceives of it as a 'social cake capable of being sliced up in different ways'[126]; intangible property that ensures a monopoly on profits included. Therefore, there seems to be some justification to expect that human sources of genetic material that are part of patents should obtain some benefit out of it, especially if they are needy in some way. But to extend such 'benefit' to control over the exercise of patent rights is not appropriate because of the uncertainty in exploitation that this will almost certainly lead to. Such control may be negotiated on the other hand as part of a benefit sharing agreement; in which case it is capable of being enforced as any other contract.

Again it is worth repeating in this context that it is in the interests of researchers and commercial entities to disclose plans of commercialisation at the time of taking informed consent or negotiating benefit sharing. Developing and developed countries must be encouraged to identify suitable terms of benefit sharing so that the distributional aspects of the commercialisation of genetic research are taken into account.

7

DEVELOPING COUNTRIES AND PATENT PROTECTION FOR HUMAN GENETIC MATERIAL

The following question was used as a guide to this section:
Do any developing or least developed countries provide or plan to provide patent protection for human genetic material. If so, what is the rationale for providing such protection?

The available information is shown in table 5. The information is adapted from a consultation document produced for the first session of a WIPO Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and folklore, earlier this year[127]. The explanations shown in the table are as presented by national governments.

7.1 Providing patent protection for human genetic material can provide a competitive edge for the industry in a particular country, but only if its technological sector is in a position to take advantage of it. There are many factors that make this especially true for the biotechnology industry. One such factor is the link between between public science and industrial technology in the case of bioindustry. In a recent study based on US patents, non patent references (NPRs) cited in patent applications were used as an indicator to quantify this link in one of the promising arenas of new drug development with startling results. The study found that patents in this area are highly science-linked, with an exceptionally large, 26 non patent references (NPRs) cited per patent. This is compared to 10 NPRs for the typical Drugs and Medicine patent issued in 1995, and an average of less than one for all patents[128].

It follows therefore that, to be competitive in the technology and derive benefit of the economic impact of biotechnology, a country would have to have competitive basic science infrastructure. In fact, in the late 80s, when the Human Genome Project was being conceptualised, it was presented to a senate hearing in the US, that only those countries who could contribute by way of basic research support for human genome studies should be allowed to benefit from commercial applications[129]. In any case it appears as though in order to provide domestic industry a competitive edge via patents (or secrecy, or non-sharing of information), a country would have to have the basic science advantage or be efficient at technology transfer. Developing countries score poorly on both counts and hence in general, there does not seem to be any particular advantage to be gained for them by providing patents on human genetic material. On the contrary, open sharing of basic information would work best in favour of developing countries that have invested in biotechnological research.

The investment in science and technology of developing countries has recently been increased in some countries. But even in the case of countries who spend a relatively high percentage of their GDP, in real terms and compared to commercial entities in the developed countries, it does not amount to very much. In Brazil, for example, the ministry of science and technology has implemented a national programme that supports scientific and technological development (PADCT). Since 1991, more than $300 million have been invested in science and technology in general of which $43 was million devoted to the biotechnology sub programme. In Kenya, the money spent

on research and development on average is 1.2 % of the national budget which is 0.47% of the GDP. In the Philippines, for 1996, the department of science and technology's institutional spending on R & D was 19.3 million. In South Africa there has been a decline in government spending on R & D which was 0.68% of the GDP in 1995.

If developing countries wanted to specifically deny protection for human genetic material, it is debatable whether and how it would be permissible under the TRIPS agreement. This question bears investigation. Art 27(1) of the TRIPS agreement requires that patent protection is available for all inventions irrespective of the field of technology. There are only limited exceptions to this requirement, and there is no explicit reference to human genetic material. Developing countries could argue that they are entitled to take such action on the basis of Arts 8 and Art 27(2).

Article 8 states that:

> Members may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development, provided that such measures are consistent with the provisions of this agreement.

The case of human genetic material is very controversial even in developed countries. The basic nature of this information has meant that raw scientific information that is as yet little understood is being monopolised. Developing countries that wanted to explicitly exclude the patentability of human genetic material on the basis of their being fundamental scientific data, the patenting of which, would be harmful for technological development would arguably be able to do so.

Article 27(2) on the other hand allows members to exclude from patentability, inventions whose commercial exploitation would damage ordre public or morality, provided that such exclusion is not made merely because the exploitation is prohibited by law. In the absence of any existing international jurisprudence on the interpretation and application of morality within patent law, it is likely that in any disputes involving questions of morality there would be reliance on the local jurisprudence[130]. This may well work in favour of developing countries

As per the WIPO information shown in table 5, no country that responded to the questionnaire, allowed for patenting of human genetic material explicitly. But going by the developments in Europe and the United States, the way in which patents on human genetic material and/or the products derived from them can be granted is spread over different kinds of provisions and rationale. Therefore a patent system which allows for *inter alia* the patenting of products that occur naturally, and new uses of known biological material is likely to be one where inventions based on human genetic material will be patentable. Unless of course, it is specifically excluded. The countries that have such provisions are shown below.

TABLE 5

QUESTION: IS IT POSSIBLE TO OBTAIN A PATENT IN YOUR TERRITORY
(A) ON CHEMICAL STRUCTURES COMPRISING NUCLEOTIDE SEQUENCES CORRESPONDING ON WHOLE OR IN PART TO NUCLEOTIDE SEQUENCES FOUND IN ORGANISMS (EXAMPLE; CODING AND NON CODING)
(B) ON CHEMICAL STRUTURES COMPRISING AMINO ACID SEQUENCES CORRSPONDING TO PEPTIDES OR PROTEINS PRODUCED BY A NATURALLY OCCURRING ORGANISM, INCLUDING PLANTS, ANIMALS OR A HUMAN BEING?

Country	A	B	Explanation, if any given
Bangladesh	*	-	The issue is still being debated.
Brazil	N	N	
Cameroon	N	N	Not patentable under the African Intellectual Property Organisation (OAPI) system.
China	Y*	Y	Yes they are protected as chemical products
Colombia	N*	N*	For qn A and B – No, protection is granted solely to the sequences of nucleotides and amino acids that do not occur in nature or are a replica of those occurring in nature. Paragraph B of Art 6 of Decision 344, Common Regime of Industrial Property.
Cuba	N*	N	No, it is not possible to patent chemical structures comprising nucleotide sequences corresponding in whole or in part to that found in an organism.
Democratic People's Rep. of Korea	Y*	Y*	Yes, provided that nucleotide and amino acid sequences are capable of industrial application.
Ecuador	Y*	Y*	Yes, with the exception of material composing the human body and its genetic identity.
El Salvador	Y	Y	
Estonia	N	Y	
Ethiopia	(N)*	(N)*	For qn A – There is no explicit provision to this effect. But it is a matter whether such chemical structures constitute essentially biological processes or not. For qn B – There is no patent system for biotechnology in general and modern biotechnology (genetic engineering) in particular in our country.
Guatemala	N	N	

India	N/A	N/A	
Kazakhstan	Y	Y	
Madagascar	Y	Y	
Malaysia	(Y)*	(Y)*	It is possible to get a patent in Malaysia for subject matter that is identical to that found in nature – chemical structures comprising amino acid sequences and nucleotide sequences whole or in part found in organisms including plants, animal or human being. However the protection of the above mentioned is only given if human intervention is introduced in producing such material, not merely from a known lab analysis. The plant and animal itself does not fall in this category.
Mexico	(Y)*	(Y)*	Genetic material, in as much as it is found in nature, is excluded from patentability by Art 16, paragraph II. However when it has been isolated and characterised, it is susceptible to patenting, since it is then different from that found in nature (example: contained in any vector). Peptides and proteins are patentable once they have been isolated and characterised from their natural state, and once a function has been sufficiently ascribed to them in the patent request.
Panama	Y	N	
Philippines	Y	N*	No. (Note: If no alterations done on the amino acid sequence to produce significant difference to differentiate it from the naturally occurring).
Sri Lanka	Y	Y	
Thailand	Y	Y	
Uzbekistan	(N)*	(N)*	According to standard documentation, for chemical structures comprising nucleotide sequences corresponding in whole or in part to nucleotide sequences found in an organism, or chemical structures comprising amino acid sequences corresponding to peptides or proteins produced by a naturally occurring organism, including plants, animals or human being, a patent or a provisional patent is not granted.
Venezuela	(Y)*	(Y)*	For qn A – Yes, they are patentable as long as the nucleotide sequence is codified. For qn B -Yes, it is possible to protect them; excluding those coming from human beings (Art 7, para d, ejusdem), and as long as the inventor intervenes in order to obtain the result or technical solution. That is to say that a substance found in nature that must first be isolated from its medium and characterised by the development of a process may be patented if it has not been previously identified.
Zambia	-	-	

Notations

( ) Indicates a constructed response
* Indicates additional information
-- No response to an applicable question
N/A Not applicable as reflected by Member States

8

OTHER ISSUES RAISED BY THE INTELLECTUAL PROPERTY PROTECTION FOR HUMAN GENETIC RESOURCES

The following question was used as a guide to this section:
Do current practices in the developed countries in relation to the patenting of human genetic resources raise any other issues for the people of developing countries?

8.1 The patenting of human genetic material in developed countries may impinge on public health needs in developing countries in at least two ways. Firstly, patents are increasingly being given on basic information and techniques. For example, 'ideas' are a well-known exclusion from patents in an Anglo-American context. While articulating the reason for restricting ideas from patentability, the US Supreme Court in *Gottshalk v. Benson*[131] said that such abstractions comprised the 'basic tools of scientific and technological work'. There are many critics that would use the same language today to oppose the patenting of human gene sequences[132]. Research tools in genetics like vector technology, or the onco mouse, though technical in character (as opposed to mere ideas and abstractions) are also the 'basic tools of scientific and technological work'. The secrecy and strategic behaviour associated with patenting of such knowledge undermines the norms under which academic information is freely exchanged[133]. The basic science infrastructure in developing countries could possibly suffer as a result of this.

In terms of using the research tools, the researcher in a developing country will only have to pay for it so long as the patent has been granted in her country. Such patents in developing countries are likely to be obtained only if the economic benefits of doing so are perceived to be worth the cost. So it is possible that institutions in developing countries will be able to use the information that has been patented as a research tool in the developed world. In this context, it is also recommended that developing countries should be encouraged to maintain a healthy scope for academic research, to mitigate the effect of patents on research tools granted in their own jurisdictions.

Secondly, it has been suggested in the Editorial of a recent issue of the British Medical Journal that the human genome project has the potential to widen the 'apartheid' in health care between rich and poor countries, more profoundly than anything previously seen in medicine[134]. This is largely due to the fact that most of the advances based on the human genome project, are driven by commercial interests which many critics feel are potentially at odds with wider public health interests. Undoubtedly, the human genome offers unprecedented opportunities to all countries for understanding mechanisms of disease and developing new drugs and vaccines. But whether and how fast vaccines will be developed and for which diseases depends on resources, and an assessment of profits to be made. For example the high price of the diagnostic test for breast cancer, the patent for which is held by an American corporation has provoked opposition even in Europe[135]. Another example is the development of the DNA chip that can be used to identify predisposition to disease at

an early age. Such tests, it has been suggested, may create 'boutique medicine' drugs targeted to overcome the special risks of individuals[136]. Yet another example is the outcome of research into pharmacogenomics.

Traditionally, pharmacokinetics and pharmacodynamics have described how drugs affect the physiology of the body, and they have been used to establish the dose for a given drug. The ultimate goal of advances in pharmacogenomics is to produce a genetic profile of the patient that reflects pharamacokinetic and pharamacodynamic parameters, which can then be used in diagnostic and therapeutic assessment. The Orphan Drugs Act in the US, originally developed to encourage research into rare diseases may be used to grant market exclusivity and protect pharmacogenetic understanding of conventional drugs. A similar legislation exists in Japan and Singapore. The European Orphan Drugs Regulation that came into effect in January 2000, provides a 10 year market exclusivity, waiver of registration fees and research aid for drugs used to treat rare diseases. These provisions are laudable if they do act as incentive to research in rare or developing country diseases. But as one commentator has noted in a European context, 'it seems unlikely that the large pharmaceutical companies will divert resources from other areas of research to the research of rare diseases, where even with incentives the return is likely to be limited'[137]. It has been suggested that the pharmacogenetic strategy will only work if the drug companies can charge a high enough price for their product[138]. The matter for concern in this context is that, orphan drug legislation may eventually be used to obtain protection for existing conventional drugs that failed clinical trials because of low response rates in the general population. With a better understanding of the genetic response to the drugs, they can now be targeted at specific sections of the population that are suited to them. It is likely that such specificity will allow the conventional drugs to get an 'orphan' label, and take advantage of added benefits under the legislation.

Global health should ideally be a priority that transcends national boundaries, but developments like these would lead to greater individualised care for those who can afford it, while resources are diverted from health needs of developing countries. The relevance of the scientific advances represented by the mapping of the human genome must be maintained for both developing and developed countries. The hope is that knowledge of the human genome 'will encourage some medical researchers to seek new interventions that are population based and that emphasis will be put on developing inexpensive drugs (comparable to aspirin and β blockers) and vaccines that prevent disease and disability in populations, rather than individual based designer therapies'[139]. It is recommended that attention should be paid to this deeply divisive side of advances in genetic research, and active legislative and policy measures should be taken to encourage research into the public health needs of the developing world, where 5 billion of the world's population reside.

8.2 A related point of concern is the fact that not many of the developing countries may have adequate regulations governing the ethicality of biomedical research. Even where they do exist, it may be difficult to enforce in a research context that is highly internationalised. In an international symposium held by UNESCO earlier this year, developing countries criticised the behaviour of some laboratories that conducted research into genetic resources of poor populations, and wanted an end put to what one participant referred to as 'experimental havens' by analogy with 'tax havens'. Recently, a researcher form Johns Hopkins University was among those accused of

unethical conduct in a clinical trial in India[140]. If such unethical conduct is indeed taking place in parts of the developing world, steps should be taken to put a stop to it with urgency. Research bodies, including commercial enterprises must follow comparable standards of ethicality that they would while conducting research in the developed world. This calls for greater regulation of international collaborative biomedical research, and may require international initiatives[141].

ENDNOTES

DEFINITIONS

[1] This definition is adopted from Clayton et. al. 'Informed Consent for Genetic Research on Stored Tissue Samples' JAMA 1995 Vol. 274 no: 22, pp 1786-1792.
[2] ibid. p 1787.
[3] CIOMS, International Guidelines for Ethical Review of Epidemiological Studies, Reprinted in 19 L. Med. & Health Care 247, 251 (1991).

INTRODUCTION

[4] Literature pertaining to the struggle between developed and developing countries over the protection of intellectual property in general and patents in particular in relation to the TRIPS agreement is prolific. For example see, Samuel Oddi, 'TRIPS- Natural Rights and a 'Polite form of Economic Imperialism' 1996 Vanderbilt Journal of Transnational Law, pp 415-470; Kongolo, 'The International Intellectual Property System and Developing Countries Before and After the TRIPS agreement: A Critical Approach', 3 International Public Policy Studies 1, 1998; Calestous Juma, 'Intellectual Property Rights and Globalization: Implications for Developing Countries' at http:// www.cid. harvard. edu/cidtech/home.htm.
[5] Foreword, 'Human Genome 1991-92 Program Report' p 111. United States Department of Energy, Office of Environmental Research, Washington DC, 1992.
[6] For a discussion of what the human genome project means and the promise of better health it holds out see, 'David Cole, 'The Genome and the Human Genome Project', in Ted Peters (Ed.) *Genetics: Issues of Social Justice* (The pilgrim press, Cleveland, Ohio 1998) pp 49-70; Alison Abbott, 'Genetic Medicine Gets Real' Nature vol. 411, pp 410-412 (2001).
[7] See Heller and Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research' Science 280, pp 698-701 (1998).
[8] This is reflected in a report published by the Science and Technology Committee of the UK House of Commons on 'Human Genetics: The Science and its Consequences' (Science and Technology Committee, 1995) which says, 'We note the general agreement among our witnesses, including pharmaceutical companies and the Bioindustry Association, that fragments of genes, or genes of no known function, should not be patentable. We conclude – only a combination of a gene and a known utility which is novel and not obvious should be patentable in the context of that utility; and a combination of the same gene and a further novel utility should also be patentable'.
[9] Venter et al. 'The sequence of the Human Genome' Science 291: 1304 (16 Feb 2001).
[10] See Caskey et al. 'HUGO statement on patenting of DNA sequences' Genome Digest, pp 6-9.
[11] Some critics believe that the accurate way to understand this is to dissociate the tangible physical entity in the human genetic material from its informational value. Therefore, extra-corporeal DNA becomes a *res* but only the physical element is a matter of property, the informational element being the common heritage of mankind. See Byk, 'Patenting Human Genes' (1994) 5:4 International Journal of Bioethics 301 at 305.

[12] Thomas *et al.* 'Ownership of the Human Genome', Nature Vol. 380, pp 387-388 (1996)
[13] See Siobhan Yeats, 'The EPO's Position: The Patentability of Genomics-based Inventions' Global Patent Management, Oct 2001, pp 30-32.
[14] http://www.uspto.gov
[15] Au-Young et al. (Incyte) 5,817,479, 'Human Kinase Homologs' Oct 6th 1998. *Cf.* John Barton, 'Patents in Genomics and Basic Research: Issues for Developing World Health' Oct 1, 2001 (On file with the author).
[16] A patent granted in 1998, EP-B-630 405, whose function was assigned on the basis of computer analysis was recently revoked for lack of inventive step and lack of industrial application in view of Rule 23e(3) European Patent Convention. See Siobhan Yeats, n 13 above at p 32.
[17] Geertrui Van Overwalle, 'Patenting of Genetic Material' Temporary Committee of Genetics, European Parliament, 15 June 2001.
[18] Paul Haycock, Chairman of the British Bioindustry Association 2000, says that 'The BIA is committed to open and responsible research and information sharing programmes that take into account regulatory guidelines, the recommendations of ethics advisory boards within industry and government and a full and open debate with wider audiences'. See Paul Haycock, 'Patents in the Life Sciences' Patent World April 2001 pp 28-31 at p 31.
[19] World Health Organisation. *World Health Report 2000* Geneva WHO, 2000.
[20] See Tzotzos and Skriabin (Ed.), *Biotechnology in Developing Countries and Countries in Economic Transition,* (Wallingford 2000).
[21] Bloom and Trach, 'Genetics and Developing Countries' BMJ 2001; 322: 1006-10007 (28 April).
[22] See HUGO Statement on Patenting of DNA Sequences – In Particular Response to the European Biotechnology Directive' April 2000.
[23] See Monday 7th May 2001, *www.Human genome,* Daily News.
[24] ibid.

1

[25] Henry Greely, 'Informed Consent, Stored Tissue Samples, and the Human Genome Diversity Project: Protecting the Rights of Research Participants' in Robert Weir (Ed.), *Stored Tissue Samples: Ethical, Legal and Public Policy Implications* pp 89-107 (University of Iowa Press, 1998).
[26] See Chee Heng Leng et al. 'Bioethics and Human Population Genetics Research' Chapter 3, *Proceedings of the Third Session of the International Bioethics Committee,* UNESCO Sept 1995.
[27] Samir Brahmachari, 'Human Genome Studies and the People of India' Paper presented at the International Bar Association, Human Genome Treaty Symposium, Oct 21, 1996 Berlin.
[28] See Nature *News* 410, p10 (2001).
[29] Carol Jenkins, quoted in The Detroit News, 20 April 1996. *Cf.* Alain Pottage, 'The Inscription of Life in Law: Genes, Patents, and Bio-politics' 1998 Modern Law Review Vol. 61, p 740.
[30] US Patent Application 05397696, granted 14 March 1995.
[31] For more information on the response to the Human Genome Diversity Project see, Posey and Dutfield, *Beyond Intellectual Property: Towards Traditional Resource Rights for Indigenous Peoples and Local Communities* (International Development Research Centre, 1996) at p 162-174.
[32] ibid. at p 171.

[33] See Baird et al. 'Whose Genes are they Anyway?' Report of the HRC Conference on Human Genetic Information July 1995.
[34] Illustratively, John Liddle, Director of the Central Australian Aboriginal Congress expressed his view on the patenting of human genetic material in this way, 'Over the last 200 years, non aboriginal people have taken our land, language, culture, health – and even our children. Now they want to take the genetic material which makes us aboriginal as well'. RAFI Communiqué *The Patentability of Human Genetic Material* Jan/Feb 1994.
[35] See Andrew Hacking *Economic Aspects of Biotechnology* (Cambridge University Press, 1986) pp 43-44.
[36] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions.
[37] See Brian Martin, 'Against Intellectual Property', Journal of Intellectual Property Rights, Vol. I pp 257-270 (September 1996). See also, Richard Dunford, 'The Suppression of Technology as a Strategy for Controlling Resource Dependence' Administrative Science Quarterly 32: 512-525.
[38] By the patent information system I mean the basic data supplied by patent offices and value added data provided by private services.
[39] This measure is different from the 'bioethical labelling' recommended by the Parliamentary Assembly of the Council of Europe in Recommendation 1468 (June 29, 2000), although the motives behind it is shared. This proposal was made by Rapporteur J F Mattei in his 'Biotechnologies' report, 5 May 2000, Doc. 8738. The 'bioethical labelling' measure as proposed by him would be a guarantee that for all products derived from living matter, via biotechnologies, 'they comply with the principles laid down in the Declaration of human rights and International instruments inspired by it'. Such a measure would be analogous to the use of 'labelling' by the International Labour Organisation as a method of combating child labour. The recommendation of the current report is directed at the patent system and is more appropriately a demand for greater information, and hence not strictly a label. It is interesting to refer to analogous measures in the context of protection of traditional knowledge and genetic material under the Convention for Biological Diversity. For example the Swiss government initiative 'building a New Partnership: Draft Guidelines on Access and Benefit Sharing Regarding the Utilisation of Genetic Resources' Annex to WIPO/GRTKF/IC/1/9. Article 14 of these guidelines recommends that one viable means to foster mutual trust and confidence between stakeholders under the Convention of Biological Diversity would be to create a system of certification, which would confirm the abidance to the guidelines by the stakeholder being certified. The Draft Guidelines have been discussed on several occasions including, the 2nd meeting of the Panel of Experts on Access to Genetic Resources and Benefit Sharing (Montreal, March 2001) see document UNEP/CBD/EP-ABS/2/INF/1.

2

[40] See Jay katz 'The Consent Principle of the Nuremberg Code: Its Significance Then and Now' in Annas and Grodin, *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation* (Oxford University Press 1998) pp 227-239.
[41] International Bioethics Committee, Working Group on Population Genetics, 'Bioethics and Human Population Genetics Research' UNESCO, Proceedings of the third session, Vol. I September 1995 at p 44.

[42] See Gerald Dworkin, *The Theory and Practice of Autonomy* (Cambridge University Press, 1988)
[43] See Chapter 2, section 1 'Fundamental Principles of Research on the Human Genome', June 14 2000, Council for Science and Technology, Bioethics Committee, Japan.
[44] The HGDP's Proposed Model Ethical Protocol is a set of proposed guidelines for collecting DNA samples. 'It deals expressly with the ethical and legal issues that are raised when a project seeks DNA explicitly from populations, not individuals, especially when those populations may be scientifically unsophisticated and politically vulnerable' Preface, Houston Law Review 1431-1473 (1997), at p 1442. Similarly, the International Bioethics Committee says that 'It is worth noting that the need for consent to be 'informed' may be objectively impossible to achieve. Even when correct information is carefully presented in culturally appropriate ways, it cannot be guaranteed that it has been understood'. See no 41 above.
[45] The Declaration of Indigenous Peoples of the Western Hemisphere Regarding the Human Genome Diversity Project of Feb 19, 1995. 'We denounce and identify the...apparatus of informed consent as tools of legalised western deception and theft'.
[46] J W Harris uses the term, *first knowing appropriator,* to describe the first person to get hold of the human tissue knowing of its therapeutic (or scientific or technological) value. This term is an apt description because it is this 'knowledge' that sets the 'source' apart from the inventor and which is recognised by the patent system. J W Harris, 'Who Owns My Body?' 1996 Oxford Journal of Legal Studies Vol. 16, pp 55-84 at p 77.
[47] See Kerry Ten Kate and Sarah Laird, *The Commercial Use of Biodiversity: Access to Genetic Resources and Benefit Sharing* (Earthscan Publications, London 1999)
[48] Report of the Second Meeting of the Conference of the Parties to the Convention on Biological Diversity (UNEP/CBD/COP/2/19).
[49] See n 41 above, at p 44.
[50] The following discussion is adapted in large part from Prof. Harris position with respect to self-ownership of the body. See J W Harris, n 46 above.
[51] See for example, Art 21 of the Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, 1997. Art 21 says, 'The Human body and its parts shall not, as such, give rise to financial gain'.
[52] Despite several reasons for not recognising self ownership in human genetic material, some critics suggest that that individuals and communities should have property rights in their own genetic material. One such critic says that institutional systems based on informed consent actually disempower the very individuals and communities it aims to protect. See, Graeme Laurie, '(Intellectual) Property? Let's Think About Staking a Claim to Our Own Genetic Sample' Paper presented at the HUGO Satellite Meeting on Intellectual Property and Related Socio-Legal Aspects of the Human Genome Project April 23, 2001. See also Andrew Grubb, 'I, Me, Mine: Bodies, Parts and Property' Medical Law International, 1998 Vol. 3 pp 299-317.
[53] See n 46 above at p 82
[54] Deborah Baird et al. 'Whose Genes Are They Anyway?' *Report of the HRC Conference on Human Genetic Information* July 1995. 'Maori who attended both the Hui at Takapuwahia and the conference were unanimous that tissue and other body material taken from Maori belong to Maori. Maori

must always be in a position to make informed decisions as to how their genetic material is or can be used'. At p 3.

[55] See Greely, 'Informed Consent, Stored Tissue Samples, and the Human Genome Diversity Project: Protecting the Rights of Research participants' in Robert Weir Ed. *Stored Tissue Samples: Ethical, Legal and Public Policy Implications* pp 89-107 (University of Iowa Press, 1998).

[56] Art 22 of the European Convention for the Protection of Human Rights and Dignity of the Human Being with Regards to the Application of Biology and Medicine, 1997.

[57] It has been pointed out that genetic information is different from other types of personal information and merits special protection. At the same time, not all genetic information warrants the same kind of protection. Control of some genetic information is more critical for exercise of personal autonomy, and publication or disclosure of some genetic information can be more damaging or stigmatising than disclosure of other. For a discussion of the implications of the use of genetic information, see Annas et al. '*The Genetic Privacy Act and Commentary*' Final Report of a project funded by the Ethical, Legal and Social Implications of the Human Genome Project Office of Energy Research, DOE, 1995. See also Richard Ashcroft, 'Genetic Information and "Genetic Identity" in Thompson and Chadwick Eds. *Genetic Information* (Kluwer Academic/Plenum Publishing, New York 1999).

[58] Indigenous Leader's Meeting about the HGDP, Phoenix, Arizona Feb 1995. The statement was made by leaders from the US, Canada, Panama, Ecuador and Argentina.

[59] These were the words used in *Moore v Regents of the University of California* 793 P 2d 479 (Cal 1990), to dissociate the cell line that was the subject of a controversial patent from John Moore, the patient from whose cells it was developed.

[60] In general see, Jeremy Rifkin, 'The Biotech Century' pp 37-66, (Victor Gollancz 1998). See also Richard Gold, *Human Body Parts*: *Property Rights and the Ownership of Human Biological Materials* (Georgetown University Press, 1998). In biology 'reductionism' fosters the belief that the behaviour of an organism or tissue is best explained by studying its cells, molecules and atoms and describing their constitution and function as accurately as possible.

[61] See Nelkin and Lindee, *The DNA Mystique: The Gene as Cultural Icon* (W H Freeman, 1995).

3

[62] Particular mutations predisposing to breast cancer, ovarian and colon cancer have been identified through studies of Ashkenazi Jews. See Laken et al. Nature Genetics 17, p 79 (1997). Other examples for study are the Onge tribes in India who have a small Y chromosome and low sperm count, a community of 700 families in Southern India who suffer form a combination of osteoarthritis and dwarfism, and the search for genes involved in asthma in the island of Tristan da Cunha in the South Atlantic. See 'Indian Researchers Press for Stricter Rules to Regulate Gene Hunting, Nature Vol. 379, p 381 (Feb 1996); and 'Whose Genes are They Anyway?' Nature Vol. 381 (May 1996), p 11.

[63] Lehrman, Nature 389, p 322 (1997).

[64] North American regional Committee, Human Genome Diversity Project, 'Proposed Model Ethical Protocol for Collecting DNA Samples' Houston Law Review 33 (1997) 1431-1473.
[65] Australia National Health and Medical Research Council, 'Guidelines on Ethical Matters in Aboriginal and Torres Strait Islander Research' (NHMRC 1991).
[66] Indian Health Service 'Guidelines for the Collection and Use of Research Specimens' See William Freeman, 'The Role of Community in Research with Stored Tissue Samples' in Robert Weir Ed, *Stored Tissue Samples: Ethical, Legal and Public Policy Implications* pp 267-291 (University of Iowa Press, 1998).
[67] The table is adapted from Weijer and Eamnuel, Protecting Communities in Biomedical Research' Science Vol. 289; 1142-1144 (2000)
[68] See Article 6,7 and 8 of the UNESCO Universal Declaration on the Human Genome and Human Rights.
[69] Indian National Bioethics Commission, *Ethical Policies on the Human Genome, Genetic Research and Services.*
[70] Weijer and Emanuel, 'Protecting Communities in Biomedical Research' Science Vole 289; 1142-1144 (2000)
[71] See http://icmr.nic.in/guide.htm
[72] Guidelines with regard to Human Biological Material, issued by the Ministry of Health and Family Welfare, 19th Nov 1997.
[73] See http://www.autogenlimited.com.au/ethics.html
[74] See Loane Skene, 'Sale" of DNA of People of Tonga' Genetics Law Monitor March/April 2001 pp 7-9 at p 7.
[75] In Iceland, the biotechnology company DeCode is collecting information from anonymised patient records from Iceland's national health service, which covers the whole population of Iceland. See http// www. decode. com/resources/ihd/
[76] See http://www.genomics.ee/genome/actsum.html

4

[77] Opinion of the European Group on Ethics in Science and New technologies to the European Commission, *Ethical Aspects of Human Tissue Banking* 21 July 1998 para 1.10
[78] This is reflected in statements like the following: 'I would like to add that international collaboration between medical researchers, including collaboration that requires the exchange of genetic material, is a noble un-commercial activity' D Balasubramanian, 'Gene Hunting in India' [letter] Nature 380 (1996) 664.
[79] Bartha Knoppers, 'Human Genetic Material: Commodity or Gift?' in Robert Weir, Ed, *Stored Tissue Samples: Ethical, Legal and Public Policy Implications* pp 227-233 (University of Iowa Press, 1998)
[80] See 'Fundamental Principles of Research on the Human Genome' June 14 2000 *Council for Science and Technology, Bioethics Committee.* (available at www.mext.go.jp/a_menu/ shinkou/principles.htm)
[81] See part VI of the HGDP Model Ethical Protocol, Houston Law Review 1997 pp 1431-1473.
[82] HUGO Ethical, Legal, and Social Issues Committee Report to the HUGO Council, 'Statement on the Principled Conduct of Genetics Research' 21 March 1996.

[83] Faulkner, W and Senker, J *Knowledge Frontiers: Public Sector Research and Industrial Innovation in Biotechnology, Engineering Ceramics, and Parallel Computing* (Oxford: Clarendon Press 1995)
[84] Juma, 'Intellectual Property Rights and Globalisation: Implications for Developing Countries' available at www.cid.harvard.edu/cidtech/home.htm.
[85] WTO 1999. *Transfer of Technology* Communication from India. World Trade Organisation, Geneva.
[86] Carol Jenkins, 'Health in the Early Contact Period: A Contemporary Example from Papua New Guinea' (1988) 26:10 Social Science and Medicine 997. For a detailed analysis of the case of the Hagahai see Alain Pottage, 'The Inscription of Life in Law: Genes, Patents, and Bio-Politics' 1998 Modern Law Review Vol. 61, pp 740-765.
[87] T R Sivaramjani and Samir K Brahmachari, 'Human Genome Studies and Intellectual Property Rights: Whither National Interest?' Current Science, Vol. 72, no: 10 pp 708-716(25 May 1997).
[88] Nature *News* 'China Brings in Regulations to Put a Stop to Genetic Privacy' 3 September 1998.

5

[89] This was pointed out in a document prepared for the 8th session of UNESCO's International Bioethics Committee, 12-14 September 2001. See UNESCO Press 'The Human Genome and the Patent Boom Challenge' available at http://www.unesco.org/opi/eng/unescopress/2001/01-97e.shtml
[90] Nick Scott-Ram, 'Biotechnology Patenting in Europe: The Directive on the Legal protection of Biotechnological Inventions – Is this the Beginning or the End?' [1998] Bio-Science Law Review 43; See also, Edward Armitage and Ivor Davis, *Patents and Morality in Perspective* (London: Common Law Institute of Intellectual Property, 1994).
[91] Arts 52-57, EPC.
[92] The statutory backing to take account of moral and socially (un)desirable features of an invention dates from the Statute of Monopolies of 1623. This was largely declaratory of existing common law and made all monopolies null and void except as recognised by the Act itself. S.6 of the Statute, expressly limits the ambit of patentable subject matter. An initial reading shows up three prohibitions in the proviso – *so also they be not contrary to law, nor mischievous to the state (*by raising prices or hurt of trade), *or generally inconvenient.* These clauses have never been regarded as capable of illumination solely by strict etymological assessment and literal statutory interpretation. A patent text written in 1851 declares that the law would not protect an invention 'immoral in its very nature' Tanner, *The law of Patents and Registration of Invention and Design in Manufacture*, (John Crockford, London 1851).
[93] Peter Drahos, 'Biotechnology Patents, Markets and Morality' [1999] European Intellectual Property Review 441 at 443.
[94] The European Directive expresses the apparent 'neutrality' of the grant of a patent in Recital 14, where it states that European and International law will continue to apply and the requirements of public health, safety, animal welfare, ethical standards etc. will continue to be effective in restricting, prohibiting and monitoring research and use of the commercialisation of the results of the research.

[95] For an analysis along these lines, see Lane, 'Patenting Life: Responses of Patent Offices in the US and Abroad', 32 Jurimetrics Journal 89 (1991).
[96] Stephen Crespi, 'The Morality of Patenting' in Sigrid Sterckx Ed., 'Biotechnology, Patents and Morality (Ashgate 1997) pp 219-223 at p 220.
[97] See David Kell 'Treatment of Immoral Subject Matter Under Patent Law: A Historical Analysis' DPhil thesis, Oxford University 1995. He says that grant or denial of a patent exerts economic pressure. Powerful stigma may be associated with a court or administrative body finding that particular subject matter is contrary to morality or ordre public. There are reports of considerable criticism from the industry on the apparent immoral nature of the 'baldness mouse' patent. The Upjohn company's patent attorney in response to the EPO's examination report said, 'The applicant regrets having included features considered to be immoral or contrary to public order. The applicant is pleased to say that they have not transformed any mammals with oncogenic reporter genes'.
[98] See discussion of this point in Sigrid Sterckx, 'European Patent Law and Biotechnological Invention' in Sterckx Ed. 'Biotechnology, Patents and Morality (Ashgate 1997) at p 10.
[99] [1995] OJ EPO 388.
[100] Amanda Warren, 'A Mouse in Sheep's Clothing: The Challenge to the Patent Morality Criterion Posed by "Dolly"' [1998] EIPR pp 445-452 at p 446.
[101]Stephen Crespi, 'The Morality of Patenting' in Sigrid Sterckx Ed., 'Biotechnology, Patents and Morality (Ashgate 1997) pp 219-223 at p 220.
[102] Beyleveld and Brownsword, 'Mice, Morality and Patents: The Onco-mouse Applications and Article 53(a) of the European Patent Convention' (Common Law Institute of Intellectual Property, 1993) p 51.
[103] Beyleveld and Brownsword's argument in this context is slightly different and centres on exploitation of the invention, which issue I have already described in the previous paragraphs. They say, 'To allow the patent would be to put the manufacturer in a potential position to profit from his/her immoral behaviour; and it is going to be immoral to profit from this behaviour it is certainly going to be immoral to be granted a monopoly on this profit'. Beyleveld and Brownsword, 'Mice, Morality and Patents: The Onco-mouse Applications and Article 53(a) of the European Patent Convention' (Common Law Institute of Intellectual Property, 1993) p 51.
[104] European Patent Convention, Art 99(2).
[105] Van Gend en Loos (Case 26/26) [1963] ECR 1. In this case Article 12 of the EEC was implemented in light of the Preamble of the EEC Treaty.
[106] Deryck Beyleveld, 'Why Recital 26 of the E.C Directive on the Legal Protection of Biotechnological Inventions Should be Implemented in National Law' [2000] IPQ no 4, pp 1-26, at p 9.
[107] See UNESCO Document SHS/HPE/2001/CONF-804/3 *Intellectual Property in the Field of the Human Genome,* Preliminary Analysis of available documents concerning intellectual property in the field of the human genome, 30th Jan-1st Feb 2001. at p 18.
[108] Recommendation 1468 of the Council of Europe, 2000 'Biotechnologies'.
[109] This argument has been put forth in a European context by Beyleveld and Brownsword. See n 102 above.
[110] See HUGO Ethics Committee 'Statement on Benefit Sharing' April 9, 2000.
[111] See Beyleveld 'Why Recital 26 of the E.C Directive on the Legal Protection of Biotechnological Inventions Should be Implemented in National Law' [2000] IPQ no 4, pp 1-26, at p 25.

[112] This is a joint project of the Georgetown University's Kennedy Institute of Ethics and the Foundation for Genetic Medicine, which allows for the full text analysis of all DNA patents issued by the United States Patent and Trademark Office.
[113] WIPO/GRTKF/IC/1/6 April 6 2001.

6

[114] Lawton-Smith et al. 'Knowledge-complexes and the locus of technological change: the biotechnology sector in Oxfordshire' (On file with the author).
[115] For a discussion on genetic identity or genetic information see Thompson and Chadwick, '*Genetic Information'* (Kluwer Academic/Plenum Publishing, New York, 1999).
[116] See Bent *et al. Intellectual Property Rights in Biotechnology Worldwide* (1987) at p 30, Art K Rai, 'Intellectual Property Rights in Biotechnology: Addressing New Technology' 1999 Wake Forest L R 827. See also Straus and Moufang, '*Deposit and Release of Biological Material for the Purposes of Patent Procedure: Industrial and Tangible Property Issues*' (Baden-Baden, 1990), pp 95-114.
[117] Nelkin et al. describe the gene as a 'cultural icon'. See Nelkin and Lindee, *The DNA Mystique: The Gene as Cultural Icon* (W H Freeman, 1995). However there is more than symbolism that is rightly associated with genetics. Genetics has for a long time been used to legitimate inequalities between long-standing inhabitants and immigrants, different racial groups, women and men, and other groups 'facing each-other across socially erected gulfs of difference'. See Lewontin, Rose and Kamin, *Not in Our Genes: Biology, Ideology and Human Nature* (Pantheon, 1984). Joseph Straus raises the point that, from a scientific point of view it seems even questionable to distinguish genes depending on their source. He quotes Dr Bayreuther from a talk at the Heidelberg Academy of science as saying, 'there is no difference between a yeast gene and a human gene if you observe it in function, if you introduce mutations and make the yeast gene a human gene, there is no difference. There is no ethical issue on the human gene that is different from a yeast gene'. He quotes another expert as saying there is no reason to identify a gene, which expresses in the human liver as 'human'. It is appropriate to specially identify the human genome as a macroscopic structure, but to identify the source of 'little bits of DNA' whether it comes from human, plants or animals, is to give it an 'etiquette that is not appropriate'. See Joseph Straus, 'Patenting Human Genes in Europe – Past Developments and Prospects for the Future' IIC Vol. 26 no 6/1995 pp 921-951, at p 927, fn 30.
[118] See UK Human Genetics Commission consultation document 'Whose hands on your genes?'
[119] Rebecca Eisenberg, 'Re-examining the Role of Patents in Appropriating the Value of DNA Sequences', 49 Emory L J 783 (2000), at p 786.
[120] This patent covered claims *inter alia* to 'a DNA fragment encoding a polypeptide having human H2-relaxin activity'. Patent no. 11.2149. The patent was upheld in *Howard Florey/Relaxin* [1995] O J EPO 388.
[121] *John Moore v Regents of the University of California* 793 P2d 479. John Moore's spleen was diagnosed as diseased and removed on the advice of his doctors. Thereafter he learnt that his doctors had discovered an unusual protein in blood cells isolated from his spleen that may be used to develop an anti-cancer agent. An immortal cell line was developed and patented by his

doctor from the excised spleen and other extracted materials without the knowledge of John Moore, who claimed that his cells were misappropriated and that he was entitled to profits derived from the commercial use of his cells. For a critique of the legal reasoning in this case and an analysis of its adverse implications see James Boyle, S*haman, Software and Spleens: Law and the Construction of the Information Society* (Harvard University Press, Cambridge 1995).

[122] See Joseph Fondacaro, 'Protecting Patients Rights in the Licensing of Human Cells' Patent World, October 2001 pp 18-20.

[123] In general see, Jeremy Rifkin, 'The Biotech Century' pp 37-66, (Victor Gollancz 1998).

[124] David Dickson, 'Whose Genes are They Anyway? Nature Vol. 381 (1996) p 11.

[125] See 'Testing Time for Gene Patent as Europe Rebels' Nature *News* vol. 413 p 443; (2001); 'French Researchers Take a Stand Against Cancer Gene Patent' Nature *News* vol. 413, pp 95-96; (2001).

[126] Harris, 'Who Owns my Body?' Oxford Journal of Legal Studies, Vol. 16 1996 pp 55-84 at p 57.

7

[127] WIPO/GRTKF/IC/1/6 Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore, *Information Provided by WIPO Member States Concerning Practices Related to the Protection of Biotechnological Inventions.*

[128] Kroll et al. 'Tracing the Influence of Basic Scientific Research on Biotechnology Patents: A Case Study of Signal Transduction and Transcriptional Regulation (STTR)' Patent World, March 1998 pp 38-46.

[129] The primary concern for the US was Japan, who 'have a very badly funded basic science programme'. On the other hand, they are perceived as excelling at technology transfer. The fear was that Japan would not support the basic research of the HGP, but would be the first to capitalise on commercial applications. See Karen Lebacqz, 'Fair Shares: Is the Genome Project Just?' in Ted Peters (Ed.) *Genetics: Issues of Social Justice* (The pilgrim press, Cleveland, Ohio 1998) pp 82-107 at pp 84-85.

[130] Margaret Llewelyn, 'The Patentability of Biological Material: Continuing Contradiction and Confusion' [200[EIPR pp 191- 197 at p 193.

8

[131] 409 US 63 (1972).

[132] See Peter Mikhail, 'Hopkins v Cellpro: An Illustration that Patenting and Exclusive Licensing of Fundamental Science is not Always in the Public Interest' Harvard Journal of Law and Technology 2000 pp 375-393. After a critical discussion of litigation concerning technology related to stem cells, the author concludes, 'While patents may serve a critical role in facilitating technology transfer, guidelines need to be established and enforced to regulate the licensing practices of inventions funded by the NIH. Much of the research funded at the university level by the federal government is fundamental in nature and forms the basis for an unknown range of further discoveries. Inhibiting developments based upon that research is antithetical to the very purpose of sponsoring university research. Science so basic and

fundamental to the functioning and treatment of the human body should not be controlled solely by free market forces'.

[133] See Arti Kaur Rai, 'Regulating Scientific Research: Intellectual Property Rights and the Norms of Science' Northwestern University Law Review 1999, pp 77- 152.

[134] Bloom and Trach, 'Genetics and Developing Countries', BMJ 2001; 322: 1006-1007 (28 April).

[135] 'French Researchers Take a Stand Against Cancer Gene Patent' Nature *News* Vol. 413; pp95-96 (2001).

[136] Bloom and Trach, see n 134 above.

[137] See, 'Orphan Drugs Proposal' International News, Patent World Oct 1999, p 6-8, at p 8.

[138] William Evans, Chairman of the pharmaceutical sciences department at St Jude's Children's Research Hospital pointed out that, 'Pharmaceutical companies may develop a drug that only 10 per cent of the market can use, but 100 per cent of that 10 per cent will use it'. For a reference to the quote and a detailed description of pharmacogenetic developments, see, Robert Snedden, '*Pharmacogenetics Workshop Background Paper*' Wellcome Trust, Friday 29th Oct 1999, London (on file with the author).

[139] Bloom and Trach, n 116 above.

[140] K S Jayaraman, 'Johns Hopkins embroiled in Fresh Misconduct Allegations' Nature, Vol 412, p 466 (Aug 2001). The High Court in the state of Kerala in India, accepted a petition claiming that an investigational drug was injected into cancer patients at the Regional Cancer Centre in Thiruvananthapuram, the state capital, without clearance from the Drug Controller General of India, and without approval from the institutional ethical committee. The head of the clinical radiobiology section at this hospital, Dr Bhattathiri is quoted as saying, 'Such conduct in clinical trials will make kerala and India an animal house'.

[141]See, Justice Michael Kirby, 'An unofficial report on the International Symposium of UNESCO on Ethics, Intellectual Property and Genomics, *Intellectual Property and the Human Genome'* Paris 30 January – 1 February 2001.