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Should there be property rights in genes?

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SUMMARY

This paper deals with the following questions. Are there property rights in the human body or its parts? What legal control is, or should be, available in respect of genetic material? Can, or should, patents be granted for genes or for products incorporating human genetic material? How extensive are patent rights over genetic material? Should ethical matters be a critical part of the patent granting process?

1. THE NATURE OF THE DEBATE

Modern genetic engineering involves big business. Wherever important commercial interests are at stake, it is important to identify the nature and extent of relevant legal rights. Research and development in genetics has raised questions as to whether, and what, rights exist in living body material, including genes.

Until relatively recently many of the legal questions involved were not widely canvassed. They appeared to be highly philosophical and theoretical. More recently, however, there is an awareness of their practical importance. Such developments as have occurred have disclosed a fascinating intermix of ethical and legal principles.

Almost certainly, there will be litigation in the coming years over the ownership of genes. As so often happens, the precise way in which such litigation arises may be unforeseeable and surprising. Hence, in a case this year, the question arose whether the next of kin of a person had any possessory or ownership rights to their brain. In the case of Dobson versus North Tyneside Area Health Authority (Times Law Reports, July 15, 1996), a man had died of a brain tumour. His brain was removed for an autopsy, and fixed in paraffin; the rest of his body was buried. The hospital was sued for negligence for failing to preserve the brain. The Court of Appeal was reluctant to hold that there was any right of property or possession in the next of kin, since the hospital had acted lawfully. The fact that the brain had been fixed in paraffin did not transform it into an item of property in the same way as other tangible material. There was no continuing duty to preserve it and the next of kin had no right to possession. The court could not see that there was any duty on hospitals to retain tissue removed in a postmortem against the possibility that it might be material evidence in civil litigation commenced at some future time. In a more widely publicised case, attempts were made to challenge a patent issued to the US Government relating to the unique genetic material of a man from a remote part of Papua-New Guinea. The Rural Advancement Foundation International (RAFI) reported that: 'the US Government has issued itself a patent on a foreign citizen. On March 14 1995, an indigenous man of the Hagahaai people from Papua-New Guinea's remote highlands ceased to own his genetic material. While the rest of the world is seeking to protect the knowledge and resources of indigenous people, the National Institute of Health is patenting them.'

The news report states that, in fact, the patent itself showed quite a different story. It covered a cell line infected with a previously unknown variant of the human T-cell leukaemia virus. Unlike most strains, this one does not cause leukaemia and was therefore of interest to researchers. It appears to be prevalent in the Hagahaai people, who reportedly agreed to the filing of the patent application and will share in any royalties.

One commentator, in an interview with *Science* said, 'the idea that the US government owns this person or his genetic material is absolute rubbish… These donors… can continue obviously to use their own DNA… They could also, if they chose, patent anything else… that was an invention, from their DNA'.

But RAFI indicated that it proposed to use the patent as part of its campaign for future action. It 'believes that the patent is only the beginning of a dangerous trend toward the commodification of humanity and the knowledge of indigenous people. Whether human genetic material or medicinal plants are the target, there is scarcely a remote rural group in the world that is not being visited by predatory researchers. Indigenous people, whose unique identity is in part reflected in their genes, are prime targets of gene hunters. The group said that it is considering bringing the issue of human patenting to the World Court at the Hague.

Thus, there is a general question relating to legal ownership. Does the law provide that the body or its parts, whether large or small, can be 'owned' in the same way as cars and houses, and so be subject to being bought and sold?

Society and lawyers have always been uneasy about this. Ownership of other living people, slavery, was

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abolished a long time ago. Corpses are not normally the subject of ownership. There is simply a duty upon those lawfully in possession of a body (next of kin, personal representatives or hospital authorities) to provide a decent burial within a reasonable time. Legislation has been passed, almost on an *ad hoc* basis, concerning various uses of human material; for example, the Human Tissue Act (used primarily to legitimate transplantation); the Anatomy Acts; the Human Fertilization and Embryology Act. Most of these provisions seek to avoid establishing clear property rights. But are there, or should there be, any wider general rules?

Various interest groups are now campaigning, on ethical grounds, against the concept that property rights can exist in genetic material or activities associated with it. Their arguments are wide-ranging. The following are samples of these arguments: (i) 'society's relationship with nature will be reduced to a commercial enterprise based on exploitation and profit (Genetic Resource Action International (GRAIN)); and, (ii) the concept of human rights will be eroded as human beings, and parts of their bodies, become the exclusive property of patent holders. (GRAIN).

Apoteker (1996) stated that 'Granting patents on human genes and parts of the human body implies that human beings and ethnic groups are now seen as no more than a source of raw material for the biotechnological industry. How can it be morally acceptable to allow such a devaluation of humanity? Treating the gene pool as a chemical product for the benefit of private interests can hardly be considered a moral act, and certainly does not fit into the framework of relations between individuals and society, the complexities of which cannot be reduced to financial rewards or purely technical considerations.'

Life patents are not necessary for the conduct of science and technology, and may in fact retard or limit any benefits which could result from new information, treatment or product. Ethical and religious values based on respect for life, creation, and reproduction will be subverted by a reductionistic and materialistic concept.

A recent document, known as the *Blue Mountain Declaration*, states the following points.

(i) The conversion of life forms, their molecules or parts into corporate property through patent monopolies is contrary to the interests of the peoples of the world.

(ii) No individual, institution or corporation should be able to claim *ownership* over species or varieties of living organisms.

(iii) Neither should they be able to hold patents on organs, cells, genes or proteins, whether naturally occurring, genetically altered or otherwise modified.

(iv) Indigenous peoples, their knowledge and resources are the primary target for the commodification of genetic resources. We call upon all individuals and organizations to recognize these peoples' sovereign rights to self-determination and territorial rights, and to support their efforts to protect themselves, their lands and genetic resources, from commodification and manipulation.

2. THE RIGHT TO ACQUIRE AND USE GENETIC MATERIAL?

What legal rules, then, determine how human material, such as genes, can be acquired and used for research purposes?

(*a*) *The Moore case 15 USPQ 2D 1753*; *271 cAL. rPTR. 146* (*1990*)

As one would expect, the US provides the leading case so far concerning ownership of human tissue. That case concerned Mr Moore, who had a diseased spleen. The doctor who was treating him took tissue from this spleen, developed a cell line from it, which was then patented and commercialized very successfully. Mr Moore had not been told of the research interest and commercial potential of his unique tissue. When he did find out, he sued the hospital.

The court agreed with him that the doctor and hospital were at fault in not disclosing to him their research interest, and he was entitled to compensation for this failure to disclose such information. But, was he also the 'legal owner' of his tissue? If so, this might give him an entitlement to some of the profits resulting from the patent? The scientific community maintained that research and development in biotechnology would be seriously hampered if persons were to have proprietary rights in their own tissue.

The Californian court, on policy and ethical grounds, agreed: '[If the] plaintiff is permitted to have decision-making authority and a financial interest in the cell line, he would then have the unlimited power to inhibit medical research that could potentially benefit humanity. He could conceivably go from institution to institution seeking the highest bid and, if dissatisfied, claim the right simply to prohibit the research entirely.... [The] patented cell line and the products derived from it... cannot be Moore's property... It is both *factually* and *legally* distinct from the cells taken from Moore's body.'

This type of case has not yet been argued before UK courts. It raises a range of issues which have not yet been properly addressed in UK law:

(i) Should an individual (the source of the body material) have sole, or any, control over what may be done with his 'body parts' and for what purposes?

(ii) Should it be possible for any right of control to be transferred or abandoned, either expressly or by implication?

(iii) Should there be a general legal presumption, in the absence of contrary provision *or* if there are no special features (as there were in *Moore*) that material is *abandoned*, with the consequence that the material may be used for any purposes; and that its economic potential is of no concern to the patient?

(iv) What relevance, if any, are hospital consent forms? Should they advert to the possible use of discarded tissue? If so, how much information should be given to the patient?

(v) If there is a right of control over the use of discarded tissue, empowering a patient to: specify what may, or may not, be done; specify for general or

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specific purposes; require payment or a continuing economic interest?

(vi) Should a physician, in relation to any tissue taken from a patient, be required to disclose any specific research and/or economic interests?

(vii) Is there any significant difference, or should there be, between known 'unique and non-unique' material?

These and similar questions are now coming under the gaze of various committees. Thus, recently the UK Nuffield Council on Bioethics made various recommendations on this matter: the removal of tissue for research use should not be induced or encouraged by commercial considerations; tissue obtained in the course of medical treatment or from living donors should only be used for purposes for which the patient or donor has expressly or implicitly consented; medical personnel and tissue banks should supply tissue for commercial research purposes on a non profit-making basis; and so on (Nuffield Council on Bioethics 1995). Comparable provisions are being drawn up by the Council of Europe draft Convention on Human Rights and Biomedicine (1996). These include article 21: 'The human body and its parts shall not, as such, give rise to financial gain'; and article 22: 'When in the course of an intervention, any part of a human body is removed, it may be stored and used for a purpose other than that for which it was removed, only if this is done in conformity with appropriate information and consent procedures.'

If and when courts in Europe are called upon to pronounce on such matters, it is anticipated that they will strive to act reasonably. As in the *Moore* decision and in the recent brain case in the UK, it may be preferable for the courts to avoid creating artificial concepts of ownership, but rather emphasize the need for patient understanding and consent in donating human tissue subject to a general judicial control to ensure that consent cannot be given for improper purposes.

3. INTELLECTUAL PROPERTY AND GENES

Of greater relevance today, however, is the question of what rights exist in the results of research in genetic activity. Are those who do the research, and/or their paymasters (whether private companies or public institutions), entitled to own or control the research information and the processes, products and uses developed from it? These raise difficult, controversial issues of intellectual property law, particularly patents.

(*a*) *Patenting living material*

Patents are granted for 'inventions' and give the inventor a kind of monopoly right to exploit commercially the invention for periods of up to 20 years. In the *Moore* case, for example, the medicinal products which owed their origin to Mr Moore's diseased spleen, could be protected for a lengthy period.

For many years, it has been accepted that patents can be granted not only for mechanical or chemical inventions, but also for biological developments; in horticulture or agriculture, for example. As biotechnology and genetic engineering progressed, issues began to arise as to the patentability of various kinds of life forms.

(i) *The Chakrabarty ruling in the USA*

In Diamond versus Chakrabarty (447 US 303; 206 USPQ 1935 (1980)), a patent application was made for a genetically engineered microbe which could be employed to eat up oil slicks. The US Supreme Court dismissed objections that it would be inappropriate to grant rights over life forms. It emphasized that the proper distinction to be made was not between the living and the non-living but between the work of 'Nature' and the work of man. In its view, in the absence of special factors, '*anything under the sun* should be patentable if it meets the required conditions of novelty and inventiveness and is capable of industrial application.'

The Chief Justice, Burger CJ., declared: 'Scientists, among them Nobel laureates, are quoted suggesting that genetic research may pose a serious threat to the human race, or, at the very least, that the dangers are far too substantial to permit such research to proceed apace at this time. We are told that genetic research and related technological developments may spread pollution and disease, that it may result in a loss of genetic diversity, and that its practice may tend to depreciate the value of human life.

The grant or denial of patents on microorganisms is not likely to put an end to genetic research or to its attendant risks. The large amount of research that has already occurred when no researcher had sure knowledge that patent protection would be available suggests that legislative or judicial fiat as to patentability will not deter the scientific mind from probing into the unknown any more than King Canute could command the tides. Whether [the applicant's] claims are patentable may determine whether research efforts are accelerated by the hope of reward or slowed by want of incentives, but that is all…'

(ii) *The Oncomouse catalyst*

The catalyst for a fundamental examination of these issues was the *Oncomouse* patent application, the final outcome of which is still pending in Europe.

The 'Oncomouse' is a mouse specially bred to develop cancer. It was the result of experimentally introducing a cancer-promoting oncogene into mouse eggs so that the gene is carried by the resulting 'transgenic' mice; and it could be transferred to subsequent generations. These mice could be used to speed up the search for new drugs to treat cancer by allowing laboratories to test drugs against a human cancer in an animal. Accordingly, the claim was very broad and covered any transgenic non-human animal bearing an activated oncogene sequence introduced by genetic engineering techniques. In the face of opposition, a patent was granted in the USA over the Oncomouse. Also, in the face of opposition, the

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European Patent Office (EPO) granted a similar patent, but the outcome of proceedings to have the patent revoked has not yet been announced.

(*b*) *Technical patent issues and genes*

Leaving aside the ethical dimension, all patent applications must satisfy a number of criteria, of which the most important are: (i) there must be an invention as opposed to a discovery; something that has been developed as the result of some 'technical' activity of man; (ii) the invention must be new, something not publicly known in the prior state of the art; (iii) the new development must be inventive, something not obvious to persons in the relevant area of activity; (iv) the claimed invention must be capable of being reproduced from the information made available in the patent application (or from material deposited with the patenting authorities); and, (v) the invention must be capable of industrial application, some product or process which is useful in industry or commerce.

These criteria have been applied for many years by the EPO to inventions using human substances. Patents for genes and proteins obtained through genetic engineering have been granted by the EPO since 1983: they are treated as being similar to chemical products in terms of patentability. To date, over 300 patents have been granted by the EPO covering both the genes coding for human proteins and the proteins themselves, and some 2000 applications for patents have been filed. Applications for such patents are filed at the rate of about 300 per year. Between 1981 and 1995 a total of 1175 patents for human genes have been granted throughout the world.

Were the patent offices right, however, in holding that genetic engineering inventions come within the scope of patents? This is one of the matters discussed in detail in the *relaxin* decision. In *Howard Florey/relaxin* ((1995) OJ.EPO 388; [1995] EPOR 541) a patent had been granted in respect of a gene obtained from the human ovary which codes for the hormone relaxin, a substance which relaxes the uterus during childbirth. Opposition proceedings were brought by members of the Green Party. Both technical patent and ethical patent arguments were raised. The technical issues will be referred to here.

The main argument was that the application related to a discovery. If something is manufactured by man, or some type of technical activity is involved, the product or process is capable of being an invention; if something is simply found in nature, for example a new plant with medicinal properties, in that state it is simply a discovery. Life forms, such as microorganisms, are found in nature and would appear to be unpatentable discoveries; so too, the gene encoding relaxin was always present in the female human body and must be regarded as a discovery.

The EPO disagreed. Patent law has extended the concept of invention so as to include any natural substances if they have been refined, extracted or isolated. The technical effort involved in such an activity brings the living material within the scope of the patent system: the isolated relaxin gene was the product of an invention; there was novelty; and there was an inventive step.

'To find a substance *freely occurring in nature* is… mere discovery and therefore unpatentable. However, if a substance found in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if the substance can be properly characterized either by its structure, by the process by which it is obtained or by other parameters and it is 'new' in the absolute sense of having no previously recognized existence, then the substance *per se* may be patentable. An example of such a case is that of a new substance which is discovered as being produced by a microorganism.' (EPO Guidelines.)

To those who would argue that the distinction is artificial, the response is to use chemistry as an analogy: 'there is nothing new in the granting of patents for substances *isolated* from nature e.g. chemicals have been obtained from leaves of plants, proteins from animals, microorganisms from the soil. Such substances have been patented as isolated products. DNA is a chemical molecule and as such is no different from any other chemical molecule e.g. rubber or a perfume molecule.' (Evidence of British Technology Group to Human Genetics Committee.)

'Therefore, provided that… the requirements of novelty, inventiveness and sufficiency of patent disclosure are met, the DNA (the chemical substance *per se*) which represents a gene or a part of a gene is patentable under patent law, and will continue to be so, unless specific law is made to exclude it from patentability.'

(*c*) *The ethical dimension of patents*

(i) *US arguments*

Since the US is the world leader in biotechnological research and also has spawned many of the interest groups concerned with the ethics of biotechnology and genetic engineering, it was inevitable that ethical objections would be raised once patent applications began to include claims in relation to higher life forms, notwithstanding the *Chakrabarty* decision.

In line with that decision and with previous stated policy, the US Patent Office, in 1988, granted a patent for the Harvard Oncomouse (mentioned earlier), this being the first US patent for a transgenic animal. Although animal rights activists and others are continuing their campaigns, to a greater or lesser extent, against the patenting of genetically engineered animals and other living material, the US Patent Office is now granting patents regularly in these areas.

(ii) *Morality in the EPO*

The ethical dimension to patenting biotechnology has taken a different, and so far unresolved, course in Europe. Unlike US law, Article 53 (a) of the European Patent Convention (and, consequently, the patent laws of all Member States of the Community who adhere to the Convention) contains an express provision that patents shall not be granted in respect of 'inventions the publication or exploitation of which would be

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contrary to *ordre public or morality*'. It had been thought that this provision would be applied only in very rare situations. Patent Office Guidelines suggested that it would be applicable in extreme cases, such as an application for a letter bomb; and a few attempts had been made to use morality arguments when opposing early attempts to patent contraceptive substances and devices.

Choice 1: the '*balancing*' approach

Article 53 (a) has now become a major weapon in the armoury of the opponents of patents on life forms. Its first significant appearance was in the *Harvard Oncomouse* application where it was argued that, quite apart from technical patent objections, the EPO should call in aid Article 53 (a) and reject the application on morality grounds.

The European Patent Office agreed that it would consider the ethical issues relating to the proposed use of the Oncomouse and decided that the benefits and burdens should be weighed up. Having carried out this exercise the Office nevertheless concluded that the patent should be granted since, in its view, the activity was ethically acceptable: transgenic mice to be used for cancer experiments were useful to mankind; the animals presented no risk to the environment and the invention contributed to the reduction of overall animal suffering since the number of such animals required was smaller than the number of conventional animals which would otherwise be used. In a later case, however, the Patent Office rejected a similar application for a transgenic mouse patent where mice were to be used for testing cosmetics: the benefit for mankind was not sufficient.

There were many criticisms of the Patent Office for adopting this approach: the patent system is the wrong place to regulate ethical and moral matters; patent examiners have no special expertise or right to consider the ethical propriety of a particular inventive development; if these duties have to be undertaken by the Patent Office it will lead to increased cost and delays in the patenting of biotechnology (which is particularly true now when pressure groups are objecting to biotechnological patents as part of their general campaign strategy); the ethical debate should be conducted in a wider arena; a refusal by the Patent Office to grant a patent on morality grounds does not mean that such inventions cannot be developed and exploited (it simply means that there will be no monopoly rights over such innovation, so that anybody will be free to develop and exploit the subject matter of the invention); refusal to grant patents is discriminatory *vis a vis* inventive activity in other technological and industrial areas and will affect research and investment; the alternative to animal patents—trade secrecy—will reduce competitiveness.

Choice 2: the '*light-touch*' approach

More recently, however, a more cautious approach towards the morality question was adopted by the Office. In the first case (*Plant Genetic Systems NV* (1993) 24 IIC 618), Greenpeace opposed a granted patent involving the insertion of a gene into plant cells encoding a particular type of protein and making them resistant to herbicides. This time, the Opposition Division resisted the invitation to balance the social and ethical benefits and burdens of this activity. The European Patent Office, in its view, was not a proper forum for discussing the pros and cons of the genetic engineering of plants in general or the present plants in particular. The claim that the patenting of higher life forms is in principle unethical was a philosophical argument which could not be accepted in the absence of any standards of absolute morality. It also refused to consider arguments that such activities posed threats to the environment: the fact that there might be deficiencies in the regulatory framework did not vest the European Patent Office with authority to carry out the regulatory tasks.

A similar line was taken in the *Relaxin* case, although the Opposition Board did examine the various arguments advanced to demonstrate the immorality of the activity.

First was the claim that since the DNA relaxin gene could only be isolated from the tissue of a pregnant woman, the use of pregnancy for profit was an offence against human dignity. However, the Board noted that the original ovarian tissue had been donated during the course of necessary gynaecological operations and so the use was no more immoral than using donated blood as the source of life-saving substances, such as blood clotting factors.

The second argument, that to patent genes amounted to slavery contrary to the fundamental human right to self-determination, was met by the Board's response that the opponents had fundamentally misunderstood the nature of a granted patent: a patent does not give the proprietor any right over a human being but merely the right to prevent another from practising the same invention *outside* the human body.

Third, the Board rejected the claim that to patent human genes was patenting 'life' and therefore intrinsically immoral. In its view DNA is not life but rather a chemical substance which carries genetic information to produce medically useful proteins.

'It cannot be overemphasized that patents covering DNA encoding human H2-relaxin, or any other human gene do not confer on their proprietors any rights whatever to individual human beings… No woman is affected in any way by the present patent – she is free to live her life as she wishes and has exactly the same right to self-determination as she had before the patent was granted. Furthermore, the exploitation of the invention does not involve dismemberment and piecemeal sale of women. The whole point about gene cloning is that the protein encoded by the cloned gene… is produced in a technical manner from unicellular hosts containing the corresponding DNA; there is therefore no need to use human beings as a source for the protein. The only stage at which a woman was involved was at the beginning of the making of the invention as a (voluntary) source for the relaxin mRNA.' In this rather strongly worded

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decision, the European Patent Office refused to draw any distinction in principle between the patenting of genes and the patenting of other human substances that might be useful in treating humans.

Of particular interest, however, was not that the Board had responded to some of the ethical arguments, but rather that it confirmed that the European Patent Office's general approach to the immorality exclusion in Article 53 (a) of the European Patent Convention would remain that as set out in its Guidelines, namely, not to balance the competing interests, but rather to avoid the ethical debate save where the general public would consider the invention *so abhorrent* that patenting would be inconceivable.

No final decision has yet been taken in the European Patent Office as to whether it should generally adopt the 'balancing exercise' approach or the 'light-touch' approach of only interfering in extreme cases. More guidance may come from the office as the result of further proceedings in relation both to the *Harvard Oncomouse* and *Relaxin* decisions.

It is submitted, however, that the latter approach is more appropriate. To add to the burdens of patent office examiners the task of dealing with all the ethical and social arguments relating to developments in biotechnology at a time when many interest groups may find it convenient to air their public concerns through the medium of the patent process may be time consuming, expensive and a possible deterrent to research and development in areas which are not otherwise prohibited or fenced off by legislative or ethical bodies exercising wider social functions.

4. OWNERSHIP OF GENE SEQUENCES AND OF GENETIC INFORMATION

(*a*) *The HUGO patent story*

There has, of course, been a quite separate, and no less contentious, issue relating to the patenting of genes: whether, and at what stage, the information and genes unravelled in the various genome mapping projects can be patented, or otherwise protected by intellectual property law.

The patent controversy relating to the 'human genome project' began in 1991 when the US National Institute of Health (NIH) and its employee, Dr Craig Venter, filed the first of many patent applications in respect of thousands of sequences of DNA from brain cells. These small cDNA fragments (expressed sequence tags (ESTs)) had been newly isolated, but the complete gene sequences and their function in the human body were not then known.

The filing of these applications incurred the displeasure of much of the international scientific world. For example, the French National Consultative Committee on Ethics condemned this patenting policy, emphasizing that the information contained in the human genome forms part of the common heritage of humanity; an area of knowledge which cannot be made the subject of a monopoly.

It is important to identify precisely the nature of the objection. It was not, in most cases, to the patenting of useful benefits derived from genetic information. The patenting of complete gene sequences whose function in the human body is known and which can be isolated and translated into therapeutic products of commercial value, as has already been discussed, was acknowledged by most scientists in this area.

The fundamental objection, based upon a mixture of ethical and technical factors, was that patent applications were being made in respect of partial genetic sequences (these included both ESTs and sequence tagged sites (STSs)) whose *function* in the human body *was unknown* and where there were *no known useful benefits* immediately arising from such information. The applications raised overlapping questions as to whether the claims were being made for discoveries or inventions and whether it could be shown that the partial genetic sequences had sufficient 'utility' to meet patent requirements. If partial gene sequences have no known use, then we have simply information or discoveries, without any utility.

In the USA, the Patent and Trademark Office rejected the claims on various grounds: attempts were made to meet some of the doubts expressed about these applications by specifying possible uses: as forensic markers for personal identification or as diagnostic markers for disease: for identifying human brain tissue; creation of probes; antisense oligonucleotides and vectors for gene fragments; and marking particular human chromosomes. These uses were not acceptable: some lacked utility; some were 'vague, indefinite, misdescriptive, inaccurate and incomprehensible'; some that they did not adequately define the invention or provide enough information to enable others to repeat what the applicants claimed to have done; and also that some were obvious. Similar objections to partial gene sequences were upheld in European patent offices; and HUGO has also confirmed the ethical position: 'Raw human genomic DNA sequences, in the absence of additional biological information and demonstrated utility, is inappropriate material for patent filing.... [Access] to the initial genomic sequence as it is generated will provide the maximum opportunity for research and for development of new products.'

Thus the 'human genome' controversy relating to the patenting of sequences, a controversy which also served to focus attention upon this difficult dividing line between discovery, information and invention, has now quietened down and any perceived threats to scientific research have also receded.

(*b*) *Other intellectual property rights in genomes*

The genome databases contain vast, and constantly increasing, stores of information. Commercial organizations ordinarily would expect to exercise control over access to, and use of, such information: they are the results of their economic investment. Such organizations, and indeed, academic institutions could protect their investment in these databases by seeking the assistance of other types of intellectual property law, such as copyright and related rights. This can be effected by a combination of copyright law and a new *sui generis* right (created by a recent European Database

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Directive) conferred upon owners of databases to prevent unauthorized extraction and reutilization of information from a database.

The Human Genome Organization, however, whilst reaffirming the role of patenting with regard to new processes and products using genes, has maintained that all sequence information should be in the public domain to provide the maximum opportunity for research and development of new products: the human genome is part of the common heritage of humanity.

The following principles were endorsed in February 1996 by all HUGO participants, including officers from, and scientists supported by the Wellcome Trust, the UK Medical Research Council, the USA National Institute of Health, the National Center for Human Genome Research, the US Department of Energy, the German Human Genome Programme, the European Commission, HIGH and the Human Genome Project of Japan. It was noted that some centres may find it difficult to implement these principles because of legal constraints and it was therefore important that funding agencies were urged to foster these policies.

(i) *Primary genomic sequences should be in the public domain*

It was agreed that all human genomic sequence information, generated by centres funded for large-scale human sequencing, should be freely available and in the public domain in order to encourage research and development and to maximize its benefits to society.

(ii) *Primary genomic sequences should be rapidly released*

Sequence assemblies should be released as soon as possible. Finished, annotated sequences should be submitted immediately to the public databases.

It was agreed that these principles should apply for all human genomic sequences generated by large-scale sequencing centres, funded for the public good, in order to prevent such centres establishing a privileged position in the exploitation and control of human sequence information.

In order to promote co-ordination of activities, it was agreed that large-scale sequencing centres should inform HUGO of their intention to sequence particular regions of the genome. This information will be presented on HUGO's World Wide Web page which will direct users to the Web pages of individual centres for more detailed information regarding the current status of sequencing in specific regions. This mechanism should enable centres to declare their intentions in a general framework, while also allowing more detailed interrogation at the local level.

5. THE PROPOSED DIRECTIVE ON THE LEGAL PROTECTION OF BIOTECHNOLOGICAL INVENTIONS

(*a*) *Clarifying and strengthening technical patent law*

In 1988, the European Commission introduced a Proposal for a Directive on the Legal Protection of Biotechnological Inventions designed to clarify this area of the law. The original Proposal was concerned almost exclusively with technical patent matters and was silent on the morality of patenting in the area of biotechnology. However, from 1992, many interest groups in the European Parliament and elsewhere focused attention on the ethical issues and the original technical and commercial objectives of the Directive became overshadowed by them.

In early 1995, after seven years of controversy, extensive discussions and many revisions to the document, the European Parliament rather surprisingly rejected the proposed directive. Undeterred by its defeat, the European Commission presented a fresh proposal for a directive in December 1995 which seeks to take account of the calls by the European Parliament for clarity and more precision, particularly in connection with the ethical guidelines.

On the technical patenting side, the Commission attempted both to clarify the rules and to emphasize, in resounding tones, that parts of the human body (including genes) should not be patentable in their natural state. Thus, it seeks to clarify the distinction between patentable inventions and unpatentable discoveries; so the earlier ban on patenting 'parts of the human body…*as such*', which involved disputes as to the precise meaning of the term *as such* has been clarified. Now, 'the human body and its elements *in their natural state*' are not to be considered patentable inventions whereas 'an element isolated from the human body or otherwise produced by means of a technical process shall be patentable, even if the structure of that element is identical to that of a natural element.'

The distinction between discoveries and inventions is referred to both in the Recitals and the Articles: The Recitals state:…(13) Whereas it should be specified that knowledge relating to the human body and to its elements in their natural state falls within the realm of scientific discovery and may not, therefore, be regarded as patentable inventions; whereas it follows from this that substantive patent law is not capable of prejudicing the basic ethical principles excluding all ownership of human beings.…(15) Whereas therefore it should be made clear that an invention capable of industrial application and based on an element isolated from the human body or otherwise produced by means of a technical process is patentable, even where the structure of that element is identical to that of a natural element, *since no patent may be interpreted as covering an element of the human body in its natural environment forming the basic subject of the invention*.

Article 3 provides: (i) 'The human body and its elements in their natural state shall not be considered patentable inventions'. The Commission explains this once again: [This] draws the distinction between a discovery and an invention…[Patentability] applies to something that is artificial in the sense that it is a technical solution to a technical problem and has been invented by man. Conversely, a discovery concerns something natural. The need to draw a clear distinction provides the justification for referring, in the second paragraph, to a technical process in contrast to what is natural. Thus the words *in the natural state* are used to

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stress that elements of the human body are to be treated as discoveries and not to be considered as inventions.'

(ii) Notwithstanding paragraph 1, the subject of an invention capable of industrial application which relates to an element isolated from the human body or otherwise produced by means of a technical process shall be patentable, even if the structure of that element is identical to that of a natural element. The Commission's comment here is that: '[This paragraph] stipulates that biological material of human origin may form the subject-matter of an invention. This provision is necessary in order to make clear that elements of human origin must satisfy the conditions governing patentability before they can be considered inventions.'

(*b*) *Dealing with the ethical issues: ethics and gene therapy*

On the ethical side, this latest proposal not only acknowledges the importance of public policy and morality in relation to biotechnological inventions but also specifies that 'it must be determined whether applications offend against public policy and morality in each specific case, by means of an appraisal of the values involved, whereby the benefit to be derived from the invention, on the one hand, is weighed and evaluated against any risks associated therewith and any objections based on fundamental principles of law, on the other hand.' Thus, the 'balancing approach' as applied in the *Harvard Oncomouse* case is preferred to the *Relaxin* approach of interfering only in extreme, abhorrent, applications. Although the proposal claims to provide an illustrative list of inventions excluded from patentability so as to provide national courts and patent offices with a 'general guide' to interpreting the reference to public policy or morality, it in fact offers very few guidelines, save in the area of gene therapy.

(i) *Somatic cell gene therapy*

Somatic cell gene therapy, which involves alteration of genes of somatic cells in an individual patient with the intention of alleviating disease in that individual alone, seems to pose no special ethical problems for the Commission: products or processes concerned with somatic cell gene therapy can in principle be patented

(ii) *Germ-line therapy*

Germ-line therapy, which involves the modification of germ cells containing DNA which will be transmitted to, and so affect, future generations, is much more controversial. For example, the purpose of gene modification of sperm or ova or cells which produce them would be to prevent the transmission of defective genes to subsequent generations. Some would prohibit all such activity. Article 13 of the Council of Europe draft Convention on Human Rights and Biomedicine (June 1996), provides that: 'an intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.' The UK National Academies have stated that intervention in the human germ line could not be justified at the present time or in the foreseeable future. Others are less certain and would postpone decisions until more was known, for example, by restricting such research at present to germ-line manipulation of animals.

Germ-line gene therapy patents would also raise interesting issues as to the scope of the rights of the patent owner. If a patented gene is inserted into humans and is then transferred down the generations can it be said that the patent holder has monopoly rights over such persons and their descendants for as long as the gene is protected by a patent?

Technically, of course, the monopoly right in a patented gene would extend down the line, albeit for a limited time. However, the control would only arise in connection with any commercial use of the patented gene; for example, if a nursing woman whose mother milk has been enriched by the insertion of a patented gene in her mammary glands sold the milk, or where a person sells egg cells (ova), sperm or blood incorporating a patented gene that can be used, say, to manufacture a vaccine. However, if a patented gene is inserted into a person's sex cells and passed on to the next generation, there would be no infringement by a person having children who had acquired the relevant gene, provided the activity was not commercial! Whilst this could not be regarded as ownership of a person, it would certainly involve a form of limited control.

All such problems are likely to be side-stepped: the proposal for a 'biotechnology directive' provides that methods of human treatment involving germ-line gene therapy are to be considered unpatentable. Also to be considered as unpatentable are 'processes for modifying the genetic identity of animals which are likely to cause them suffering or physical handicaps without any substantial benefit to man or animal, and also animals resulting from such processes, whenever the suffering or physical handicaps inflicted on the animals concerned are disproportionate to the objective pursued.' The group of advisers on the 'ethical implications of biotechnology' of the European Commission has recently (1995) given cautious approval to the principle of genetic modification of animals.

It is likely that the European Commission will seek a speedy adoption of this directive. Although there appears to be rather more common ground than heretofore between the various interest groups involved, it remains to be seen how easy it will be to adopt these proposals. Of course, even were the proposal to be adopted in its present form, not all the technical and ethical issues relating to patentability in the biotechnological and pharmaceutical industries will have been resolved. For example, some scientists still maintain that intellectual property control over aspects of gene technology will inhibit research activity and could block off whole areas of important scientific research and development; others respond by pointing out that such a fear applies in respect of the entire patent system, and has not materialized. The British Technology Group (1996) memorandum states: 'Another complaint is that if a company has a patent on, say, hepatitis C genes, no one else can do research

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in that area. This is incorrect: experimental (research) use of a patented process is not an infringement. What normally happens is that such research results in an improvement, which can also be patented. The first company in the field will need the improvement, while the second company needs to be able to operate under the main (first) patent. The two normally come to terms by cross-licensing each other under the main and improvement patents. The system has worked very well, not least in the US which has a flourishing biotechnology industry.'

6. SOME CANVASSED REFORMS RELATING TO GENES

Alongside the various proposals for clarifying and restating the law in the proposed biotechnology directive, other suggestions for reform of the law have been made in connection with genes and related patents.

(*a*) *Rewards for those involved in pure genetic research*

Suggestions have been made that some lesser form of protection should be introduced which would give limited rights over the discovery of genetic information when that information is subsequently put to commercial use. This is not a problem that is limited to biotechnology research, however, and the proposed solution would be difficult to apply in practice, in the absence of appropriate contractual rights.

(*b*) *Patenting of genes*

Those who still remain unhappy about rights in genetic material have canvassed a number of suggestions to restrict the scope of patenting in this area.

(i) *No patent on genetic material?*

Should there be a prohibition against the patenting of all human genetic material, even though it otherwise met the existing requirements for patentability? This has been strongly opposed by various sections of industry, arguing that Europe would be put at a major competitive disadvantage *vis à vis* the US and Japan where patenting of isolated human genes is accepted, and it is unlikely that this proposal would be taken further.

(ii) *No patents on naturally occurring genes, even if isolated?*

As a possible variation of the above, could a distinction be drawn between genes synthetically made, which would remain eligible for patent protection, and naturally occurring genes isolated from the body, which would not be eligible?

This suggestion has come from the Danish Patent Office, which maintained that there would be no major impact upon the interests of industry since once a gene has been isolated and characterized it can subsequently be manufactured synthetically in modified form. Thus, in applying this to the *Relaxin* patent, the Danish Patent Office report stated: 'the *naturally occurring* preprorelaxin gene from humans was isolated and characterized. The characterization of the gene makes it possible to manufacture a *synthetic* form containing the same genetic information. Based on the synthetic gene, relaxin is manufactured by genetic engineering means. One of the advantages of the invention is that relaxin can be manufactured in greater quantities than is possible by isolating the hormone from humans. The [Danish] Patent Office considers the identification of a naturally occurring gene that codes for preprorelaxin a discovery. But isolation and characterization of the gene, and utilization of the knowledge thus obtained to manufacture a synthetic gene—and, on the basis of this, the hormone relaxin—is an invention. It is this invention for which the European Patent Office has granted a product patent. According to the [Danish] Patent Office, however, this patent takes in both the naturally occurring gene and the gene in synthetic form; and an improvement would be to limit rights to the latter.

The essential legal implication of the patent is, therefore, a disclaimer of any rights over the naturally occurring gene. The exclusive right would be confined to 'the synthetic gene and the commercial application thereof for the manufacture of synthetic relaxin.'

In the view of the [Danish] Patent Office Report there should be no significant effect upon industry: '…industry's need to obtain a patent for the form of a gene naturally occurring in humans and hence to obtain sole rights on the commercial application thereof must be assumed to be very small, once the gene has been isolated and characterized. The gene can subsequently be manufactured synthetically in modified form. Re-isolating and using the natural gene is then of no technological and economic interest.'

However, industry did object. '[It] will lead to fierce debate about what is excluded. Will functional but non-coding parts of genes (such as promoters) be patentable? What about sequences closely similar to, but not identical with, those in nature? What about combinations of natural genes or parts of them (e.g. cDNAs which code for useful therapeutic proteins?) All of these might be excluded from patentability (although new, inventive, and perhaps exceptionally useful) by a rule which says that genes may not be protected. Resulting uncertainty will be as damaging as the loss of protection.' (T. Roberts's evidence to UK House of Commons Human Genetics Committee.)

(iii) *No patents for gene products, only genetic processes?*

Should there be a prohibition against the patenting of genetic products, such as genes, whilst allowing related processes to be patented? Industry strongly opposed this, too. Process patents are not as valuable as product patents: they are more difficult to police; they would provide inadequate protection for industry; and, where the invention consists of identification and isolation of useful DNA, the process for its commercial preparation is a matter of routine and may not meet

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the requirement for an inventive step. This would remove incentive from commercial companies to research in these areas, or even to develop the products of others' research (including academic research).

This view was shared by the UK House of Commons Human Genetics Committee which commented that 'any erosion in patent protection for products of a particular type e.g. human genes, enzymes, proteins, will effectively preclude the commercial viability of development of such products as pharmaceuticals. In view of such profound implications, considerable caution should be exercised when considering the exclusion from patentability of any subject matter or technology that could advance the frontiers of medical science such as DNA and genetic technology…'

It would seem that none of these possibilities attract major support and almost certainly would affect research and investment in European biotechnology.

7. CONCLUSION

Many of the issues relating to patent and other ownership of human body material, including genes, have not yet been resolved. There will be continuing uncertainties for some time to come. Some of the technical uncertainties in connection with patents may well be clarified by a new European Biotechnology Directive. But many of these technical matters seem to be inextricably linked to ethical questions.

Continuing uncertainty creates difficulties for everybody, and it is very important that some consensus is established as soon as possible. If any decision is taken to impose further controls on intellectual property laws, such controls should be carefully circumscribed so as not to impose unnecessary fetters upon developments in genetic engineering. Otherwise, exclusions from patentability could lead to wider constraints which could have very serious effects upon the biotechnology industries, research and development, and the welfare of us all.

In that regard, it is appropriate to notice, and to welcome, the recent creation in the UK of a Human Genetics Advisory Commission (UK), a strategic group of eminent independent members, charged with the tasks of keeping under review scientific progress at the frontiers of human genetics and related fields; reporting on issues arising from new developments in human genetics that can be expected to have wider social, ethical and/or economic consequences, for example, in relation to public health, insurance, patents and employment; and advising on ways to build public confidence in, and understanding of, the new genetics. There are already bodies of this kind, such as the Nuffield Council on Bioethics. However, an additional governmental advisory body which will keep in touch with public views on human genetics and also keep abreast of developments in other countries, can only be for the good.

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