Chapter 3

Patenting DNA
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3.1 In Chapter 2, we accepted that, in general, the application of the patent system in the field of biotechnology and biomedicine is justifiable as a way of striking a reasonable balance between the rights of inventors and the public interest. In this chapter we address the special questions which arise regarding patents that assert rights over DNA sequences. Such patents raise a number of ethical concerns, which can be divided into three types of argument, namely that:

i) patents that assert rights over DNA sequences, in particular human DNA sequences, should not be allowed by virtue of the special status or nature of DNA;

ii) patents that assert rights over DNA sequences should not be allowed because they do not meet the legal criteria for patenting;

iii) patents that assert rights over DNA sequences should not be allowed by virtue of the possible deleterious consequences for healthcare and research related to healthcare.

3.2 We consider the first two of these arguments in this chapter. In Chapter 4, we address the third argument by introducing a number of case studies to illustrate the possible deleterious effects of allowing patents with claims to DNA sequences. In Chapter 5, we consider, in the light of the preceding discussions, whether the current system for granting patents ought to be modified.

The special status of DNA

Genes as our common heritage

3.3 One argument about the special status of DNA focuses specifically on the proposition that human DNA has a special nature, compared to the DNA of other organisms. Many people undoubtedly feel uncomfortable with the fact that genes and their mutations can be claimed for commercial gain. It is argued that the human genome is unique and distinctive, so it should be treated differently from others such as the genomes of mice or maize, for example.

3.4 This view has been expressed by various organisations, including the Council of Europe’s Committee on Legal Affairs and Human Rights. The Committee called for the member states of the Council of Europe to strive to change the basis of patent law with respect to rights of ownership over human tissue and genes ‘into law pertaining to the common heritage of mankind’ in international fora such as the WTO. The Parliamentary Assembly of the Council of Europe, in addition, has approved two recommendations addressing biotechnology and IP.¹ Both reflect unease at the concept of patenting living matter and dissatisfaction with the existing patent system with respect to its approach to dealing with genes, particularly human genes.

3.5 The Parliamentary Assembly further proposed that national governments of the Council of Europe’s member states should strive for universal acceptance of a new system termed a new ‘World Patent Convention’, to be established under the auspices of an international institution or organisation. It recommended that the proposed system be founded on a principle of common heritage, which mirrors the language of UNESCO’s Universal Declaration

on the Human Genome and Human Rights (1997) in referring to the human genome as the ‘common heritage of humanity’.

3.6 References to the common heritage of humanity are easy to understand in the context of shared natural resources such as land or oil. The precise nature of the special status of the human genome is harder to elucidate. Nonetheless, it remains the case that many people feel that genetic information in humans warrants special treatment. Some claim that there should be no property rights in genes; others claim that, while there may be property rights relating to genes, such rights should be the subject of shared public ownership rather than being in private hands. We now consider each of these arguments in turn.

**The inalienable nature of genes**

3.7 There is an important fundamental constraint on individuals’ property rights, namely the respect they owe to others as persons entitled to live a life of their own. This implies, among other things, that people may not be owned by others as slaves. It is argued that this inalienable right to self-ownership brings with it an inalienable right to ownership of one’s body, including one’s genes. Thus it could be argued that no one can own, or have property rights over, another person’s genes; and this principle is widely affirmed – as in Article 5 of the EC Directive 98/44/EC:

(1) The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.’

The problem with this argument is that patents with claims to DNA sequences do not entail ownership of genes as they occur in our bodies – they relate instead to the isolated versions of such sequences which are held to be patentable. Thus, Article 5 continues:

(2) ‘An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.’

Much of the difficulty of the question of patenting DNA is encapsulated in the problem of understanding how these two principles can be consistently combined. In the present context, what matters is that Article 5(2) is taken to legitimate, for example, patents on diagnostic tests based on genes, which give the owners of patents control over the way in which use is made of knowledge about genes which are common to everyone.³ We consider the possible undesirable consequences of this situation in Chapters 4 and 5.

**Genes as public property**

3.8 The second argument is that genes, if they are to be the subject of property rights, should be publicly rather than privately owned. The concept of public property or common heritage has applied, in legal and political terms, to such things as the navigable waterways,

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2 As at June 2002, five Member States of the European Union had fully implemented the Directive: Denmark, Finland, the UK, Greece and Ireland. The provisions made in the Directive have been endorsed into the EPC under a new chapter entitled ‘biotechnological inventions’.

3 It should be noted that under most patent systems, an individual could use knowledge about their own particular genes when those genes had been patented by others, without infringing, provided that it was done in private and for purposes which were not commercial. See for example, the UK Patents Act, 1977, Section 60, Meaning of infringement.
Genes as discoveries

3.9 We suggest that this second concern about rights of ownership under the patent system is rooted in a deeper belief that genes are naturally-occurring entities that are there to be discovered, like new species or new planets. They are not invented. In our common usage of the term, a ‘discovery’ is the acquisition of knowledge of a new but already existing fact about the world. An ‘invention’, on the other hand, is something that someone creates or develops which did not previously exist. Thus, on the usual interpretation of the words, it seems apparent that the identification of a gene is a discovery, since genes exist in the world, in our bodies.

3.10 In Europe and most other countries, patent law explicitly excludes discoveries from qualifying for the grant of a patent. In the US, although the patent statute states that both discoveries and inventions qualify, in practice the law does not permit the patenting of natural phenomena. However, under the law in Europe and the US, a discovery that has a useful application may merit consideration as qualifying for the grant of a patent if it is part of an invention.

3.11 In the present context, however, the important point is that patent offices maintain that the DNA sequences claimed in patents are not natural phenomena. Instead, they say, patents that assert rights over DNA sequences do not relate to genes as they occur naturally, but rather to genes that have been isolated. That is, although these DNA sequences do in fact match the sequences of our genes, they are only patented in the context of molecules which have been artificially created by cloning and are isolated from the human body. This thesis brings us to the question of the eligibility of DNA sequences for patenting. (Box 3.1 explains how patents can assert rights over DNA sequences).

Eligibility

3.12 In discussing whether DNA sequences are eligible for patenting, we begin by summarising the legal framework in the US and Europe with regard to the patenting of DNA, and set out

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4 See for example Hardin G. The tragedy of the commons. Science 1968;162:1243-1248.
5 Title 35 U.S.C. § 101 states ‘Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.’ However, the Supreme Court has held that patent protection is not available for ‘laws of nature, natural phenomena, and abstract ideas.’ Diamond v Diehr, 450 U.S. 175, 185 (1981).
6 This is the distinction drawn in the EC Directive quoted in paragraph 3.7 above; note that Article 5(1) refers to an unpatentable discovery, whereas Article 5(2) concerns patentable inventions.
Box 3.1: Patents and DNA

Are there different types of patent?
Patents can be divided into three categories, though these categories are not formally distinguished in the patent system. A product patent is a patent on the product itself. The term ‘product’ normally means a chemical or biological entity, substance or composition (as distinct from a device or electrical circuit). A patent that asserts rights over a product itself covers all uses of that product. A process patent is a patent on a method or process. This covers a process, and may also include what is directly produced from the process. If a product is made by another process, not covered by the patent, it does not infringe it. A use patent is a patent on the use of the product for a specific purpose; only the specified use is covered. For example, in relation to a particular pharmaceutical product, a product patent would cover the active ingredient, further product patents may cover particular formulations, process patents would cover making the active ingredient or formulation, and use patents would cover the use of the drug for a specific medical indication. An important feature of product patents is that they extend to new uses of the invention that developed subsequently, even if these uses were not anticipated or predicted by the owner of the patent.

What types of patent can include assert property rights over DNA sequences?
Of the three main kinds of patent, product, process and use patents, only product patents can assert rights over DNA sequences themselves. Use patents only extend to the use of the sequence. In practice, use patents may also restrict access to the DNA sequence itself (see paragraph 5.24).

What kind of products can include DNA sequences as part of their claims?
Various products can include DNA sequences. For example, diagnostic tests that are used to determine whether an individual has a particular genetic variant. Some medicines are developed from proteins, which are produced by a gene. A patent on the medicine may assert rights over the DNA sequence that is needed to generate the protein.

How are patent applications constructed?
Patent applications generally include the following sections:

i) Abstract: A summary of the application;

ii) Description: A description of the invention, such that another person skilled in the art could produce the same invention using this information;

iii) Claims: A definition of the precise scope of the patent, in other words that over which rights are asserted. Some claims are called ‘dependent’ claims because they are based on another claim. All claims must be clear, complete and supported by the description of the invention. We use the word ‘claim’ in this technical sense in this Paper.

Why is the scope of a claim important?
The claims contained in a patent are the most important element, since they determine the limits of the monopoly, and therefore dictate what the owner of the patent can prevent others from doing without permission. Claims can be either broad or narrow, and a single patent application will usually contain claims of both sorts. As the names suggest, broad claims contain less detail than narrow claims, and therefore give the owner of the patent protection over a wider range of activities. Broad claims will generate more commercial advantage, but may be more susceptible to attack. When patents are challenged, each claim is assessed independently, so that even if a broad claim is rejected, a narrow claim may be upheld. Patents which contain broad claims are often referred to as broad patents.

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In what form do genes or DNA sequences appear in patent claims?

Patent claims may assert rights over DNA in various ways, for example, they may claim one or more of the following:

- the DNA sequence, whether comprising a complete or partial gene
- promoters
- enhancers
- individual exons
- expressed sequences as expressed sequence tags (ESTs) or cDNAs
- whole transcribed genes as cDNAs
- individual mutations known to cause disease
- variation between people not associated with disease (polymorphisms)
- cloning vectors, formed from bacterial DNA, which are used to replicate DNA sequences
- expression vectors, also formed from bacterial DNA, which are used to express proteins in replicated DNA sequences
- isolated host cells transformed with expression vectors, which are cells that have been created to express particular proteins
- amino acid sequences (proteins)
- the use of such proteins as medicines
- antibodies, which are used as markers
- nucleic acid probes, which are fragments of DNA that are used to locate particular parts of DNA sequences
- methods of identifying the existence of a DNA sequence or a mutation or deletion in an individual
- testing kits for detecting genetic mutations
- whole genomes

1 The term composition of matter patent is sometimes used in the United States to refer to a patent on a chemical product. Confusingly, it has been used in relation to both individual substances and true compositions of two or more substances.

2 An exception is first medical use patents. These are patents on products that are not novel in themselves, but for which no medical use has been previously described. This kind of patent exists only under European patent law. The claims cover manufacture of the known product for all medical uses.

3.13 As we have indicated, substances as they occur in nature and natural phenomena are not eligible for patenting as such. However, processes involving living organisms and versions of natural products which have been isolated have been held eligible for patenting in various countries for many years. There are many examples of patents granted on isolated natural products and they include Louis Pasteur’s 1873 patent on isolated yeast, granted in France and the US, a patent on isolated vitamin B12 held by the pharmaceutical company Merck &

7 Brazil is an exception in that its patent law prohibits patents on natural living beings, and biological material including genomes or germplasm of any natural living being whether found in or isolated from, nature. However, genes that have been modified may be eligible for patenting under Brazilian law (Section 1, Article 10 IX of Industrial Property Law No.9279/96).
The ethics of patenting DNA

Co (and upheld in Merck & Co., Inc. v Olin Mathieson Chem. Corp., (1958) 253 F.2d 156, 161, 163), and patents on isolated adrenaline.\(^8\)

3.14 In the UK, the 1949 Patents Act was interpreted by the UK Patent Office to mean that the first person to discover and isolate a natural substance could be granted a patent. This was a change from previous policy, which had only allowed substances to be patented if they were created by some particular method of synthesis. In 1988, before the patenting of DNA sequences had become widespread, the EPO, USPTO and Japan Patent Office (JPO) issued a joint statement clarifying the position with regard to isolation:

"Purified natural products are not regarded under any of the three laws as products of nature or discoveries because they do not in fact exist in nature in an isolated form. Rather, they are regarded for patent purposes as biologically active substances or chemical compounds and eligible for patenting on the same basis as other chemical compounds."\(^9\)

On this basis, isolated genes are deemed to be eligible for patenting despite their origin as products of nature.

3.15 As well as isolated natural products, living organisms and processes which involve living organisms can also be eligible for patenting. When plants and animals are naturally-occurring species, ‘wild’ flowers and animals as we commonly say, there is no question of anyone gaining exclusive patent rights over them. In fact, many of the plants and animals that we encounter have, however, been domesticated by breeding and hybridisation. There is a long tradition of providing incentives to plant breeders through a regime of rights to IP.\(^10\) This reflects the long-standing and widespread acceptance that the work of plant breeders merits encouragement through such a regime.

3.16 Perhaps the most well-known example of a living organism which was granted a patent is the genetically engineered bacterium that was the subject of litigation in the US, Diamond v Chakrabarty (1980). By a 5-4 decision, the Supreme Court allowed the grant of the patent to stand, US Chief Justice Burger famously remarking that in principle ‘anything under the sun that is made by man is eligible for patenting.’\(^11\) Other living organisms that have been patented include yeasts, viruses, and cell lines.

3.17 European patent law relating to naturally-occurring phenomena and living organisms has evolved along similar lines (see Appendix 2). The 1998 EC Directive on the Legal Protection of Biotechnological Inventions (98/44/EC) states in Article 3 that:

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\(^8\) Louis Pasteur's patent was US Patent no. 141,072. Merck and Co's patent for vitamin B12 was issued in 1951 claiming a method of producing the pure vitamin crystal. A US court ruled that until the inventors had made vitamin B12 available to the world it did not exist, although the substance was well known to chemists in crude extracts. Jockichi Takamine obtained patents in the US, the UK and Japan for adrenaline (epinephrine) purified from gland tissue. These patents were also challenged but it was ruled that 'for every practical purpose [Takamine had produced] a new thing commercially and therapeutically.' Parke-Davis & Co. v H. K. Mulford Co., 189 F. 95, 103 (S.D.N.Y. 1911) (http://pubs.acs.org/subscribe/journals/mdd/v04/i12/html/12timeline.html (13 May 2002)).


\(^10\) In Europe, there are rules for protecting rights over registered plant varieties governed by the 1961 Union for the Protection of New Varieties of Plants (UPOV) Convention. The UPOV system is distinct from the patent system: in Europe, plant varieties created by biological techniques (‘breeding’) are excluded from patent protection and must be protected under the UPOV rules.

\(^11\) In allowing the patent to be granted, Chief Justice Burger, delivering the opinion of the court, stated: ‘the patentee [Chakrabarty] has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under §101’.
■ ‘for the purposes of this Directive, inventions which are new, which involve an inventive step and which are susceptible of industrial application shall be patentable even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.

■ biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.’

3.18 As we noted in paragraph 3.7, Article 5 of the EC Directive states that an element isolated from the human body or produced through a technical process, including the sequence or partial sequence of a gene, may be patented even where that element’s structure is identical to that of a natural element. It can therefore be seen that in both the US and Europe, DNA sequences are regarded by the law, in principle, as being eligible for patenting once they have been isolated from their natural environment. However to be granted a patent, they must meet the legal criteria of being novel, inventive and having utility or being capable of industrial application. The question of whether DNA sequences are eligible for patenting is distinct from the question of whether they meet these legal criteria. In the next section we describe how these criteria are applied with respect to DNA. Before doing so, however, we reflect on the legal reasoning which has led to the practice of regarding DNA sequences as eligible for patenting.

3.19 One common criticism of the thesis that DNA sequences are eligible for patenting is that it fails to take account of the fact that these sequences carry information: they are the body’s way of carrying information as to how proteins are to be constructed. But this kind of information, it will be said, cannot properly be patented. It may be discovered and stored on a database which carries a charge for access; but it is simply not eligible for patenting.

3.20 In considering this criticism, it is essential to distinguish two different types of information: (i) information of the kind scientists discover about a natural phenomenon; (ii) a phenomenon, natural or artificial, which is itself essentially information, in the sense that it is a code which is used to control complex activities. Let us call information in the first sense ‘scientific knowledge’ and, in the second sense, ‘genetic information’ (there are of course other types of information of this kind, but it is genetic information that is relevant here). As we have seen, scientific knowledge concerning a natural phenomenon is not eligible for patenting, since it is a mere ‘discovery’. It follows from this that scientific knowledge about genetic information which is encoded in some naturally-occurring phenomenon is not eligible for patenting as such. But it does not follow that an artificial phenomenon that does not occur naturally (such as a molecule that has been isolated and cloned) that encodes genetic information may not be eligible. This distinction may appear a fine one; but the underlying point is crucial to an understanding of the evolution of the patent system.

3.21 Patent offices take the view that extracting the genetic information encoded by a DNA sequence is not just a matter of gaining scientific knowledge about a natural phenomenon: it involves the use of cloning techniques to create an artificial molecule in such a way that it includes much the same genetic information as is to be found in the natural phenomenon. And what is held to be important here is that the scientific knowledge concerning the genetic information has been discovered through the creation of the artificial molecule. That is to say, without isolating and cloning a gene, it is not possible to identify the
sequence of bases of which it is comprised. Hence, patent offices have concluded, the genetic information is essentially part of an 'invention', a molecule which is human handiwork, and can be patented as such.

3.22 The assumption in this defence of the eligibility of artificial DNA sequences, that the isolation and cloning involved does produce genuinely new molecules of a kind which do not occur naturally, can be questioned. Furthermore, the fact that genes are essentially just genetic information makes the issue of patenting them very different from that involved in the isolation of other chemical compounds. But the procedures involved in the early days of cloning genes were certainly inventive and arduous. For this reason, patents awarded in those early days need not now be called into question.

3.23 The early days of pioneering experiments using positional cloning techniques are now history, and many DNA sequences which were produced by a combination of computational and cloning techniques have since been the subject of patent claims. Even if it can be convincingly argued that the DNA sequences were eligible for patenting, these patents should be examined in the light of the criteria for inventiveness and utility. We discuss these legal criteria below, and argue that they need to be much more stringently applied than has been the case (paragraphs 3.29 – 3.37). In Chapter 5, we consider further their application to various ways in which DNA sequences can be the subject of property rights asserted in patents.

3.24 The defence of the eligibility for patenting of DNA sequences described above (paragraphs 3.20 – 3.21) seems to us even more doubtful as a result of the increasing availability of the sequence of the human genome. Now, it may no longer be necessary to use cloning techniques to identify the DNA sequences of genes; instead they will be identified from computer databases, the cloning and sequencing having been completed previously by other scientists and placed in the public domain. When this method is used, there would seem to be no good reason for holding that a DNA sequence thereby identified is eligible for patenting, even if it were to be subsequently cloned. For, in such a case, the scientific knowledge about the DNA sequence would not be dependent upon the construction and analysis of an artificial molecule. This state of affairs, whereby patent protection may no longer be appropriate for a particular invention, despite it having been readily granted at a time when a technology was at an early stage of development, is a common occurrence in patenting (we say more about this in paragraph 3.31 where we discuss the implications of advances in techniques for isolating genes in relation to the patent system’s requirement of inventiveness).

3.25 As computational techniques replace cloning as the main route to identifying genes, the issue of the eligibility for patenting of DNA sequences needs to be reopened. The fact that DNA sequences obtained by cloning have in the past been regarded as eligible for patenting does not imply that they should continue to be eligible for patenting when they can be identified from databases constructed by others.

3.26 As we observed above (paragraph 3.18), the fact that something is eligible for patenting does not imply that it should receive a patent. It must also satisfy the further requirements of novelty, inventiveness and utility. So, we now discuss the way in which these criteria are applied to patents that assert rights over DNA sequences.
DNA and the legal criteria for patenting

**Novelty**

3.27 To fulfil the requirement of novelty, an invention must not have been previously disclosed to the public.\(^\text{12}\) But if a gene or protein is present in nature, can it be said not to be available to the public? Individual genes in their natural state are not directly accessible and additional work is required to isolate them. Is this enough to allow the conclusion that the isolation of a gene is actually deserving of recognition in the form of patent protection?

3.28 Lawyers have argued successfully that isolating a gene from its natural environment is sufficient to show that a novel product has been created. The inventor’s isolation of a gene separates it from other molecules that are naturally associated with it and allows biochemical characterisation in the form of description of the sequence of the bases.\(^\text{13}\) As we have said, a patent involving an isolated gene does not extend to the gene as it occurs naturally, but only its isolated form. However, even if it meets the criterion of novelty, isolating a gene will be only the first step in meeting the legal criteria for eligibility for patenting. Unless the inventor can also demonstrate an inventive step and a useful application of the isolated gene, a patent will not, or should not, be granted.

**Inventiveness**

3.29 The requirement for inventiveness means that applicants must be able to demonstrate that, when compared with what is already known, the claimed invention would not be obvious to ‘the skilled person’; an ordinary worker with a good knowledge and experience of the subject. The parallel requirement in US law is that of non-obviousness. It is generally the case that the more human intervention needed to produce a product, the greater the chances of it being eligible for patenting. There has been considerable debate about whether isolated DNA sequences, as they are used in diagnostic tests, medicines or as research tools, are inventive and non-obvious to the skilled worker.

3.30 Many have argued that technological advances in DNA sequencing now mean that the process of isolating a gene can no longer be regarded as inventive, as it is a routine and industrialised process even if the resulting sequence codes for a novel product. Prior to the impact of the large scale DNA sequencing programmes, genes were identified by procedures such as positional cloning and the use of protein sequences to derive nucleic acid sequences.\(^\text{14}\) These are time-consuming and labour-intensive techniques, the early application of which was viewed as inventive. The isolation and identification of a novel DNA sequence together with a use, either disclosed or predicted, was the subject of many patent applications.

3.31 Since the early 1990s, methods such as the application of *in silico* techniques have been developed. As we have seen, now that the DNA sequence of the human genome is accessible from a personal computer, a researcher can match an unknown human DNA sequence to a homologous, or similar, gene sequence in an animal genome where the function may already be known. The researcher can then file a patent application on the human sequence, based on proposed similarity of function in the context of, for example,

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\(^\text{12}\) That is, it must not have been disclosed in the prior art (35 U.S.C. 102). Also Article 54 (EPC).

\(^\text{13}\) USPTO Utility Examination Guidelines (Fed. Reg. 66: 1093, 5 Jan 2001); the EC Directive 98/44/EC Article 5(2) (See paragraph 3.7).

\(^\text{14}\) Positional cloning is the cloning of a gene based simply on knowing its approximate chromosomal position in the genome without any idea of the function of the gene.
a diagnostic or therapeutic use. These steps can be achieved in the absence of any laboratory work. However, other techniques used for the isolation of disease genes, such as linkage and association studies, continue to require significant effort on the part of researchers. This point reinforces that made earlier in connection with the issue of eligibility (paragraphs 3.22 – 3.25), but it is worth considering separately how these changes in the methods of identifying genes affect the claim that isolated DNA sequences meet the criterion of inventiveness.

3.32 At the EPO, the assessment of inventiveness relates to whether isolating a gene is something that would have been obvious to a person skilled in the art, with regard to the prevailing art at the time, irrespective of whether the sequence itself was structurally obvious or not. The EPO has recently stated that the isolation of DNA sequences that have a structure closely related to existing sequences in which the function is known, is not inventive. The in silico approach to identifying DNA sequences is therefore unlikely to provide the grounds for eligibility for patenting in Europe.

3.33 But there are important differences between the US and European approach to assessing inventiveness in respect of claims to DNA sequences. According to the USPTO, non-obviousness does not depend on the amount of work required to characterise the DNA sequence. Rather, it depends on whether a gene having a particular DNA sequence claimed as part of a patent would have been obvious to others at the time. That is, the question is asked: would the sequence of base pairs in the section of DNA have been obvious before the gene was isolated? As it will generally be difficult to predict a given sequence without the isolated gene, the US patent law allows a low threshold on the requirement of inventiveness in the case of patents relating to genes. Moreover, the existence of a general method of isolation of gene sequences is considered to be essentially irrelevant. The USPTO's view, therefore, is that establishing the nature and function of a DNA sequence by electronic means, though a trivial process, does not exclude the granting of a patent on the grounds of non-obviousness.

3.34 We take the view that, on this matter, the test affirmed by the EPO is appropriate. The test for non-obviousness used by the USPTO means that the outcome of any complex procedure which could not have been predicted in advance, however familiar the procedure, will be judged inventive. While there is a sense in which such a result is ‘non-obvious’, that is not the sense relevant to questions as to whether a patent should be granted. For example, multiplying two ten-digit numbers will generate an answer that would not be known in advance, but it is nonetheless an obvious result.

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15 In research which aims to identify a gene or a number of genes involved in a particular disease, the approach that is often followed involves linkage or association studies of affected families, which attempt to locate a region of the relevant chromosome that may contain the gene or genes in question. Once this has been achieved, it is then a matter of searching the region on the sequenced genome for causative variation in candidate genes. In its simplest form, an association study compares the frequency of a particular genetic variant in a group of people affected by a certain condition with a matched set of controls (a similar group of people not affected by the condition).

16 In the Report of Trilateral Project B3b from the European, Japanese and US Patent Offices (http://www.european-patent-office.org/tws/report/report_start_page.htm (13 May 2002)), Nov 2001, Annex 2 p.43, the EPO states that: ‘Prima facie, the routine provision of further sequences having the same general function as the known prior art sequences of closely related structure is not inventive. The structural non-obviousness is not a reason to accept an inventive step; sequences as well as all other chemical compounds should solve a technical problem in a non-obvious manner to be recognised as inventive.’

17 35 U.S.C 103 (a) ‘Patentability shall not be negatived by the manner in which the invention was made’.

18 In re Deuel, 51 F.3d 1552, 1559, 34 USPQ2d, 1210, 1215 (Fed. Cir.1995). See Appendix 2 for further details of this case.

19 In re Deuel is not expected to be followed by the EPO.
Usefulness

3.35 The third criterion that an invention must meet to be eligible for patent protection is that it must be useful. In Europe, this requirement is termed ‘capable of industrial application’. In the US, the analogous term is that of ‘utility’. It is generally assumed that industrial application is simply the European equivalent of utility. For ease of reference in this paper we use ‘utility’ to refer to both the US and the European criteria. The scope of the US criterion has recently been revised in the new Utility Examination Guidelines of the USPTO, issued on 5 January 2001. These now require an invention to show a ‘specific and substantial and credible utility’. The term credible is interpreted here as meaning that the usefulness claimed for the invention must be theoretically possible, even though it may not have been demonstrated in the claims. There has been considerable debate over whether DNA sequences in various forms can fulfil the criterion of utility. Since the development of large-scale DNA sequencing techniques over the past ten years, more DNA sequences have become available without a concomitant understanding of their function. As a result, many patent applications have been filed on genes or parts of genes without the demonstration of a ‘credible utility’. Such patent applications, involving fragments of DNA, including expressed sequence tags (ESTs) and single nucleotide polymorphisms (SNPs), whose functions are unclear, have been controversial.

3.36 While we welcome the new USPTO guidelines, we take the view that where ‘credibility’ means no more than ‘theoretical possibility’ (i.e. where something is credible simply where it is not incredible) the threshold for utility is still set too low. The current state of genetics and biochemistry does not make it difficult to suggest functions for DNA sequences that are ‘theoretically possible’, in the sense that they are not ruled out by what is already known; but this should not suffice for the award of a patent. Instead, what is required is some evidence that the DNA sequence actually has the claimed ‘specific’ utility and that the claimed utility is truly ‘substantial’. Furthermore, the utility in question should be more than a biological function such as encoding a receptor. Even if the biological function ascribed is correct, it is only a description of a fact of nature, and not a practical utility in the usual sense applied to an invented product.

3.37 Even if a credible utility is stated in a patent, if further novel and non-obvious uses for a DNA sequence are found, patent law provides that a product patent on the sequence will extend to cover the new uses, despite their not being specified in the original patent. Thus, an inventor who applies for a patent to cover the new use will have to obtain a licence from the original patent owner if he wishes to exploit his invention. In other words, the

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20 Article 52 (1) of the EPC states that European patents shall be granted for any inventions which are susceptible of industrial application, which are new and which involve an inventive step. Article 57 of the EPC states that an invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.

21 In the US the utility requirement is covered by Title 35 U.S.C. 101: Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

22 The language of Article 57 of the EPC and its national counterparts (see footnote 21 above) is literally broader in its definition of usefulness, because it refers to inventions which can be not only used, but also made, in industry. However, in practice, this is narrowly construed, so that the two criteria are equivalent. This was confirmed in a recent judgment by the English Court of Appeal (Chiron v Murex [1996] FSR 153, [1996] RPC 535).

23 There is a point to be made about the relationship between inventiveness and utility. The EPO’s criterion for inventiveness, namely something that solves a technical problem, necessarily implies a degree of utility. It has been suggested that the issue addressed by utility in the US is addressed in Europe partly through the criterion of industrial applicability and partly through that of inventiveness.

exploitation of his patent becomes dependent on the original patent. This situation is well established in the patenting of chemical compounds such as medicines. However, it has been suggested that such dependency on the exploitation of new uses of the first patent is difficult to avoid in the case of patents with claims to DNA sequences because it is difficult to ‘invent around’ a naturally-occurring gene sequence. (We consider the question of inventing around in paragraph 5.12.)

Types of DNA sequence

Background

3.38 Patent law deals with different types of claims to DNA sequences (see Box 3.1). It is now apparent that different patents that relate to the same gene often contain claims which overlap. This situation arises because a gene, which exists inside a cell as sections of DNA, is an entire functional unit, encompassing coding DNA sequences, called exons, control regions consisting of non-coding regulatory DNA sequences, and functionless ‘introns’. A gene with, for example, 15 exons could well have a separate patent claim on each of several of these exons, which would have been discovered as expressed gene fragments (see paragraph 3.40), another claim on the complete expressed sequence discovered by screening a library of expressed gene clones, a separate claim on a promoter sequence and perhaps another on a distant locus control region found to influence the expression of the gene. Each of a number of mutations found to cause disease in different individuals, or different populations, may be the subject of a separate patent claim. Until we have a full appreciation of the assembled human genome, it will not become apparent to what extent existing patent that assert rights over DNA sequence overlap each other.

Full-length DNA sequences

3.39 The most common patent applications that assert rights over DNA sequences have been for the use of genes in the diagnosis of gene-related disorders or for use in medicines, either indirectly by coding for a therapeutic protein, tangentially as a potential target in drug research, or directly, by the intended use of the gene in gene therapy. Other common applications relate to research where the DNA sequence may be used to screen for new medicines, or as markers for disease. Many patent applications claim multiple uses of a gene. Various uses of patented gene sequences are illustrated in the case studies in Chapter 4.

Expressed Sequence Tags (ESTs)

3.40 Researchers have made extensive use of partial DNA sequences or ESTs which are easily identified when particular genes are being expressed. In the 1990s, ESTs were widely used as a shortcut to identifying genes and as a means of studying gene expression. Several companies and other organisations filed patent applications claiming EST sequences in the hope that they would manage to secure exclusive rights to the whole genes at a later stage. As the biological function of these partial gene sequences was usually unknown, they were usually claimed as research tools which could be used for the identification of genes. Although the USPTO rejected a patent application for human ESTs with no known biological function in 1991, large numbers of patent applications on ESTs have since been filed. The prospect of researchers being rewarded for the routine isolation of parts of a gene in which the biological function is unknown has attracted a great deal of criticism. Many have taken the view that ESTs should not qualify for patent protection because their production is neither inventive nor useful.

25 A dependent patent is one whose exploitation would encroach upon the exploitation of an earlier patent. A dependent patent becomes independent with the expiration of an earlier patent.
3.41 ESTs are not in principle excluded from eligibility for patenting by the patent system. However, the USPTO’s new Utility Guidelines state that the subject of a patent must have a well-established utility that must be readily apparent to one skilled in the art. The 1998 EC Directive explicitly excludes the patenting of partial or entire gene sequences where the function of the DNA sequence is unknown. Very few patents on ESTs have been granted (although it is hard to obtain accurate figures because, in patent claims, EST is a term that defines how the fragment of DNA was obtained and not what it is). It appears most unlikely that further patents on ESTs will be granted because they would not meet the utility requirement.

3.42 Patents on ESTs may extend to subsequent patent applications involving full-length DNA sequences in which the biological function is known. The claims in these patents have tended to use what is called ‘comprising’ language meaning that a patent with a claim to a sequence ‘comprising’ or containing an identified EST sequence would be infringed by a patent application that claimed the full-length gene that included the EST. It has been suggested that a proliferation of patents on individual ESTs held by different owners raises the prospect of costly future transactions to collect licences together before a company could acquire the rights to develop future commercial products. This could lead to the situation where a pharmaceutical company seeking to use a protein would infringe any patents held by others that had identified ESTs present in the DNA sequence (see paragraph 5.38).

**Single Nucleotide Polymorphisms (SNPs)**

3.43 Similar concerns have been expressed over the prospect of patenting SNPs which occur in the human genome. SNPs are single base pair differences occurring at a frequency of about 1 in every 1000 nucleotides when the genome sequences of many individuals are compared. SNPs will be valuable, amongst other things, for studying the genetics of disease and the genetic basis for the response of patients to medicines. The association of SNPs with specific genes implicated in susceptibility to diseases or response to medicines will be of use primarily for the identification of new targets for drugs. Given that SNPs are tiny, naturally occurring changes in DNA that are used as markers, they have been widely thought of as scientific knowledge that should be freely available. A consortium of ten pharmaceutical companies and the UK Wellcome Trust has been established to support the creation of a SNP map of the human genome. This consortium (TSC) will accelerate the search for genes associated with disease by making the map available to all researchers. The aim is to prevent research into substantial areas of the human genome from being impeded or hindered through the lodging of claims for patents in relation to SNPs. The initiative also aims to avoid duplication of effort. However, it has been suggested that there will still be patent applications, at least in the US, on the information which links SNPs to particular genes (the ‘association’) and which would seek to protect the use of such information.
specific genetic information to infer characteristics about the organism.\footnote{See Barton J. Patents, Genomics, Research and Diagnostics. Forthcoming under the auspices of the Association of American Colleges.} Such a development is likely to be premature in that it is likely to restrict the use of genetic information that has wide applications.

**Exceptions to eligibility for patenting**

3.44 Applications for patents which involve claims to DNA sequences can be granted, as has been seen, provided they meet the legal criteria for patenting. However, there are some inventions that meet the necessary legal criteria for patentability which are excluded from patenting under various international agreements:

- The **TRIPS Agreement (Trade-Related Aspects of Intellectual Property Rights)** (1994) of the World Trade Organisation (WTO) addresses the issue of the eligibility of subject matter for patenting in Article 27. It permits the exclusion of inventions which threaten the ‘*ordre public*’ or morality. Inventions which deleteriously affect human, animal or plant life or health or which may seriously prejudice the environment may also be excluded. However, the TRIPS agreement does not address directly the question of patenting DNA sequences.

- The **European Directive on the legal protection of biotechnological inventions (Directive 98/44/EC)**\footnote{Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.} by Article 6, prohibits patents on processes for cloning humans, the modification of the human germ line, and the use of embryos for industrial or commercial purposes.\footnote{Provisions made in the TRIPS agreement and other specified international agreements take precedence over those set out in the Directive, as regards the obligations of members of the EU.} In line with the TRIPS agreement, the Directive notes that inventions should be considered unpatentable when the commercial exploitation of them would be contrary to ‘*ordre public*’ or morality.

- The EPC, in Article 53, states that patents shall not be granted in respect of:
  
  ‘(a) inventions the commercial exploitation of which would be contrary to ‘*ordre public*’ or morality, provided that the exploitation shall not be deemed to be so merely because it is prohibited by law or regulation in some or all of the Contracting States;
  
  (b) plant or animal varieties or essentially biological processes for the production of plants or animals; this provision does not apply to microbiological processes or the products thereof.’\footnote{In November 2000, the existing prohibition on patents for methods of treatment such as surgery, therapy or diagnosis, was altered, so that rather than being inventions not susceptible of industrial application, such inventions become classified as simply not patentable, like those in Article 53(a).}

3.45 How are phrases such as ‘*ordre public*’ and ‘contrary to morality’ to be understood? The EPO has defined the concept of ‘*ordre public*’ as covering the protection of public security and the physical integrity of individuals as part of society, and the protection of the environment. The case law of the EPO Board of Appeal states that the concept of morality is:

‘...related to the belief that some behaviour [is] right and acceptable whereas other behaviour [is] wrong, this belief being founded on the totality of the accepted norms which [are] deeply rooted in a particular culture. For the purposes of the EPC, the culture in question [is] defined as the culture inherent in European society and civilisation. Accordingly, inventions the exploitation of which [is] not in conformity with the
conventionally accepted standards of conduct pertaining to this culture [are] to be excluded from patentability as being contrary to morality.”34

The difficulty of defining a shared European culture should not be under-estimated. The ongoing debate about the ethical propriety of research on stem cells derived from human embryos provide a vivid example of the lack of a common set of ‘accepted standards of conduct’ on such questions.

3.46 A useful illustration of the application of Article 53 is the opposition in Europe to the grant of a patent for the ‘Harvard oncomouse’, a strain of mouse developed in the laboratory which has a predisposition to developing tumours. The USPTO granted a patent on the mouse in 1998.35 A patent application was filed at the EPO in 1985 and was first refused by the Examining Division on the grounds that animals were not patentable under Article 53(b) of the EPC.36 The applicant filed an appeal which was successful, and in 1992 the patent was granted. Subsequently, 17 Oppositions against this patent were filed, most concerning animal welfare. The Examining Division was thus required to consider whether Article 53(a) applied. To do this, it engaged in what was an essentially consequentialist analysis, weighing the suffering of the animal and the possible environmental risks against the potential benefits to humanity. The EPO concluded that the patent should stand. It noted that, if restrictions on particular technologies were called for, this should be dealt with by legislation, not through the patent system. It also stated that three different interests had to be balanced: ‘a basic interest of mankind to remedy widespread and dangerous diseases’, the protection of the environment ‘against the uncontrolled dissemination of unwanted genes’, and the avoidance of cruelty to animals.37

3.47 Applying this approach, the Examining Division found that the invention was unquestionably of value in the development of treatments for cancer. It also noted that the use of the oncomouse would reduce the number of animals required in research, that animal models of cancer were generally considered indispensable, and that the risk to the environment was small. Finally, it stressed that these considerations only applied to the case in question and that other transgenic animals might not be eligible for patenting under the morality clause. In general, the EPO takes the view that each case must be assessed individually to ascertain whether it falls under this clause.

3.48 We note that the scrutiny of patent applications by reference to their being contrary to morality or ‘ordre public’ requires expertise in areas that may not be represented in patent offices. These areas include moral philosophy, environmental ethics and public policy. For this reason, groups such as the European Group on Ethics, have called for independent ethical evaluation of patent applications in controversial areas, such as stem cell technology.38 We recommend that the European Patent Office (EPO) should consider producing further guidance which clarifies the principles set out in Article 53(a) of

35 The USPTO has subsequently issued numerous patents on transgenic mice as models of specific pathologies, including a mouse that develops an enlarged prostate gland; transgenic mice depleted in mature T-cells; a virus-resistant mouse that produces beta-interferon, and a mouse that displays the amyloid deposits typical of Alzheimer’s Disease. See Woessner W. Patenting Transgenic Animals. J of the Patent and Trademark Office Society 2001;83:830.
36 See paragraphs 2.18 – 2.21 for an explanation of the system for opposing patents at the EPO.
the European Patent Convention (EPC) concerning patents that are contrary to morality or ‘ordre public’. We recommend that the EPO seeks general guidance from the European Group on Ethics (EGE).

Summary

3.49 In this chapter, we have considered the question of whether DNA sequences should be eligible for patenting. We draw an important distinction between the acquisition of knowledge about the nature and function of a DNA sequence, and the information contained within that sequence. Even though we think that the judgement that isolated DNA sequences are eligible for patenting is based on a questionable extrapolation to the case of genetic information from the case of the isolation of chemical compounds, we accept that a limited number of the early patents granted on that basis need not now be called into question, in view of the inventiveness required to isolate the DNA sequences. Since the early days of the pioneering experiments using positional cloning techniques, patents have been filed on many DNA sequences which were mass-produced by a mixture of computational and cloning techniques. Even if it can be convincingly argued that these sequences were eligible for patenting, the patents should be examined in the light of the criteria for inventiveness and utility. We note that as techniques have advanced, and in particular as the use of computers to identify genes has become more widespread, the eligibility of DNA sequences for patenting should have diminished.

3.50 With regard to the legal criteria for assessing patents with claims to DNA sequences, while we accept that the test of novelty can be met, the tests of inventiveness and utility are more problematic. In the case of inventiveness, we hold that as the use of computational databases becomes the standard way of identifying genes, it is difficult to see how the test can be met, despite current US practice. In the case of utility, we argue that the standard of credibility required for a claimed utility needs to be set higher than the mere theoretical possibility of this utility; some positive evidence that the DNA sequence has the claimed utility should be required. Finally, we consider the requirement that patents should satisfy the condition of not being contrary to morality or ‘ordre public’, and suggest that patent offices should seek general ethical guidance, as necessary, from relevant bodies.