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PATENTING THE HUMAN GENOME

Master Thesis

Research Programme
Innovation Markets
- Biotechnology

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Intellectual Property Rights
Spring 1999

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ACKNOWLEDGEMENTS

I would like to thank the following persons for their contributions to the preparation of this work. First of all I would like to thank Johan Förander for helping me to find an interesting subject. Furthermore I thank Dan Henriksson at Awapatent in Malmö and Monica Sundgren at the Swedish Patent and Registration Office for their excellent service in helping me find relevant material. I would also like to direct special thanks to Barbro Wedell and other people at the Department of Pathology, Institute for Laboratory Medicine at the University of Gothenburg for giving me comments on the section relating to DNA. However, any mistakes that might remain are entirely mine. I am also very grateful to Sara Mazetti-Nissen at SM-N Illustration & Media, Malmö for taking her time to make the illustrations in this work. Finally I would like to thank my supervisor, Professor Hans Henrik Lidgard for useful comments and support.

ABBREVIATIONS

CAFC	US Court of Appeals for the Federal Circuit
cDNA	complimentary DNA
DNA	deoxyribonucleic acid
ECHR	European Convention on Human Rights
EIPR	European Intellectual Property Review
EPC	European Patent Convention
EPO	European Patent Office
EST	expressed sequence tag
EU	European Union
HGP	Human Genome Project
HUGO	Human Genome Organisation
IIC	International Review of Industrial Property and Copyright Law
JPO	Japanese Patent Office
JPTOS	Journal of the Patent and Trademark Office Society
MRC	Medical Research Council (UK)
mRNA	messenger ribonucleic acid
NIH	National Institutes of Health (US)
NIR	Nordiskt Immateriellt Rättsskydd
SNP	single nucleotide polymorphism
TBA	Technical Board of Appeal (EPO)
TRIPs	Agreement on Trade-Related Aspects of Intellectual Property Rights
UPOV	International Union for the Protection of New Varieties of Plants
USC	United States Code
US PTO	United States Patent and Trademark Office

ABSTRACT

In these days there is nothing unusual about the patenting of human genes. Patent offices in the US, Europe and Japan have been granting patents for genes for over a decade. Biotechnology, being key for many industrial sectors, is today one of the most rapidly developing technologies. As any other industry, it needs protection for its inventions. Without such protection, there would be less investment in the high-risk research necessary for the development of biotechnological inventions. A healthy industry is material for economic progress in any country. Certainty about the conditions for patentability is therefore important to attract venture capital to the domestic industry. The US has traditionally been the world leader in biotechnological research, with Japan coming second. However, with the biotech industry asserting it needs a level playing field, Europe has, through the new Biotechnology Directive, taken steps towards narrowing the competitive gap between itself and the US and Japan.

There are about 100 000 genes present in the human genome. The genetic information is translated to amino acids, through the genetic code. Amino acids are the building blocks of proteins, which play many different roles in the organism. The information contained within the gene can be used in the development of pharmaceuticals, gene therapy and diagnostic methods. As with any other patent application, an application for an invention relating to a gene must satisfy the three basic criteria of patentability: novelty, inventive step and industrial applicability. (In the US the requirements are novelty, nonobviousness and utility). Furthermore, an invention must be disclosed in such a way that a person skilled in the art can reproduce it without undue effort. The current policy is to treat human gene sequences like chemical substances. Thus, for the gene to be considered as an invention, and not as a discovery, it must be purified and isolated from its natural surroundings. The contribution to the art lies in making the gene available in a form that can be used in industry, e.g. in the production of a pharmaceutical product.

Inventive step is often the most problematic condition for patentability. Since genes are treated like chemical compounds, the test in the US has often been whether or not the gene is obvious in the light of structurally similar compounds found in the prior art. However, many hold that the structural similarity criterion leads to the wrong results. The argument is that a disclosure in the prior art of an amino acid sequence can render the corresponding DNA sequence obvious, since they are linked via the genetic code. Thus, the European and Japanese patent offices generally consider a DNA sequence to lack inventive step if the corresponding amino acid sequence is disclosed in the prior art.

In order to receive a wide scope of protection, many applications claim not only one DNA sequence, but also all the analogs of that sequence. The question is then how much information about those sequences that needs to be disclosed in the application. Court decisions in the US have generally required the applicant to disclose how to make and use enough sequences to justify the grant of the claims sought. The European Patent Office has traditionally taken a more pragmatic approach, providing a larger scope of protection. According to some EPO decisions, it might be sufficient to disclose how to prepare just one sequence in order to claim a group of analogs.

However, some recent decisions show a more stringent standpoint. The general test is, after all, that a person should be able to reproduce the whole invention claimed from the description in the application.

Much of the controversy surrounding the human genome patenting has been due to patent applications relating to so-called expressed sequence tags (ESTs). An EST is a short fragment of a gene. However, since an EST only encodes part of a protein, often with unknown function, it has been held that it does not meet the utility criterion. Other concerns have been that a patent to an EST might block-off the future patenting of the full-length gene and that it might restrict downstream research by creating too many proprietary constraints. However, it has been made clear both in the US and in Europe, that if the gene can be seen as novel and nonobvious in the light of the EST patent, it would still be considered patentable. The first EST patent has now been granted, claiming the EST as a tool to find the full-length gene.

The far-reaching possibilities of modern biotechnology have increased the risk of achieving inventions that are ethically unacceptable. However, this can be dealt with by the specific exclusionary provisions have been introduced into the patent systems. Europe and Japan have specific statutory clauses prohibiting the patenting of inventions, the exploitation would be contrary to ordre public or morality. In addition, the EU Directive has introduced certain exemptions to patentable subject matter, which are directly relevant to biotechnological inventions. The US deals with such issues on a case-law basis. The rationale behind such moral provisions is to prevent the impression being given that an invention, whose use would be contrary to legal fundamentals or offend the sense of decency, bears the seal of society's approval. However, one important court decision from the EPO has verified that the patenting of human genes cannot generally be considered as immoral.

A different issue is the question concerning ownership of parts of the human body. Does a person own the parts of his or her body? If human tissue is used for commercial purposes without the permission of the donor of that tissue, is this theft of that person's property? A US court decision has established that the donor of tissue does not have any right in a patent to an invention developed from that tissue, even if the donor had not given consent to such conduct. The court stated that if the donor were to be granted property rights in anything developed from such tissue, it would inhibit research to the detriment of society. The societal interest in protecting the biotechnology industry from possible lawsuits relating to proprietary issues was thus considered being of greater importance than the individual's interests in his excised tissue.

1. INTRODUCTION

Biotechnology is a field that is capable of evoking mixed emotions. This is particularly the case when the discussion encompasses the subject of human genome research. On the one hand there are major benefits that can spring from the studying of human genes. On the other hand it has been met with many moral and philosophical disagreements. Accompanying the debate about biotechnology itself has been a debate about whether the products thereof should be patentable. The Human Genome Project, although not yet complete, has provided scientists with vast amounts of DNA sequence information, further highlighting the issue of the patentability of the human genome. As any other field in technology, genetic research need protection for new inventions and has therefore turned to the patent system. Biotechnology is a high-risk industry and investors need a reasonable guarantee to get a proper share of the commercial benefits that are expected to flow from the research. The significance of gene patents lie thus in its ability to attract venture capital to the biotechnology industry. Even internationally there is fierce competition on who is going to attract more investment to the country's biotechnology industry. The country with the most effective means to ensure sufficient protection is likely to get ahead in the race. But due to the controversial nature of patenting human genes there is also a need to strike a balance between economic and ethical goals. Human genome patenting is giving rise to concerns both at a popular level and within the scientific community.

This work focuses on the legal and social concerns that surround the patenting of human genes. The aim is to explain how and why patents have become an important element in the research of the human genome, as well as the implications hereof. I will look at the situation in the US and Europe, with some comments on Japan. I have chosen to concentrate on these legal systems since most of the genetic research is done here. Giving a brief description on each of these patent systems, I will point to the differences and the similarities between them. Moreover, I will recount for the development towards the patenting of genes, explaining what makes a gene a patentable invention. Going through each of the requirements for patentability, I will account for how DNA can fulfil these requirements. I will also examine problems that may appear and discuss whether the patent system is suitable for protecting human material, taking a look at alternative methods of protection. However, to get a well rounded view I believe it is important to look beyond the most immediate topic and into adjacent areas. Thus I will incorporate an economic and ethical dimension into the legal analysis. Since law is not an isolated phenomenon in society I believe this is necessary to gain a deeper understanding of the forces that shape the law.

I will concentrate rather strictly on the patenting of DNA per se and therefore I will not touch upon other related areas, such as process patents and the patenting of other biological materials. Focusing mainly on the requirements and the process to obtain a patent protection, I will leave possible consequences, such as infringement procedures and technology transfer agreements, aside.

My approach will be one of a mainly descriptive and comparative method, however with some attempts of basic analysis. The material I've used has been gathered mainly from legal and scientific journals. Much of the sources are American since

the US is clearly the world leader both in the area of biotechnology research itself and in the inclination to patent its findings. But with the new EU directive on the protection of biotechnological inventions, the activity in the biotech patent realm has gathered momentum also in Europe.

2. THE HUMAN GENOME

The complete set of instructions for making an organism is called its genome. Found in the nucleus of each cell, the genome is the totality of the information contained in the chromosomes. The human genome is estimated to comprise at least 100 000 genes.¹ Most people know that genes transmit hereditary characters from one generation to the next as well as direct several other processes in our bodies. But where exactly are our genes situated, what do they consist of and what is it more specifically that they do? In this section I will explain the basic character and function of our genes, giving you enough information to be able to follow the next chapters.

2.1 The gene and its functions

The genes are responsible for the genetic information that determines hereditary traits as well as controlling other biological processes in our bodies by directing the production of proteins. These proteins are largely responsible for the structure and the function of the organism. Proteins are large, complex molecules composed of long chains of amino acids. The human body can synthesize at least 100 000 different kinds of proteins.² It is the genes that determine the composition of the proteins by coding for the amino acids. Proteins play many roles in organisms. Some proteins make up structural components of the organism; for example the protein collagen is preset in our bones. Others perform particular functions; one example is the protein hemoglobin that transports oxygen in the blood, another example is the proteins of the immune systems, which protect against diseases. Another group of proteins is the enzymes, which functions as biological catalysts.³

Genes are contained in long DNA molecules, which in turn are part of the chromosomes present in the cell nucleus. The human genome is estimated to consist of about 100 000 genes. All the cells in the body contain the same genes but due to the specialization of cells, different genes are “active” (expressed) in different cells, depending on the function of the cell. Thus, for example, a bone-marrow cell expresses certain genes, whilst a brain tissue cell expresses others.

¹ US Department of Energy, Primer on Molecular Genetics, p. 7 found at www.ornl.gov/hgmis/publicat/primer/intro.html.

² Department of Energy, Primer on Molecular Genetics, p. 7.

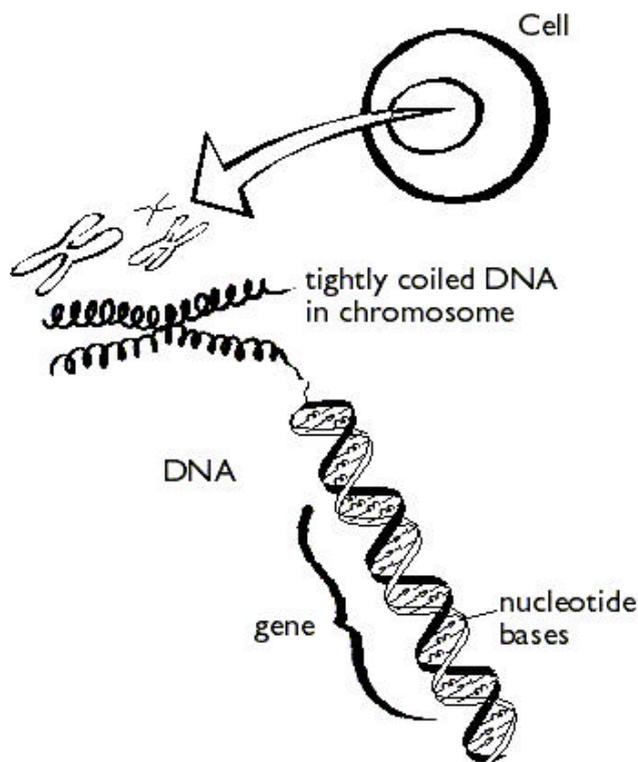
³ Britannica Macropaedia, Vol. 19, p. 710.

2.2 DNA

The DNA has two important functions. One is to express the genetic information carried in the form of a chemical code by directing which proteins to produce. The other function is to replicate itself in the process of cell division.

2.2.1 DNA as an information carrier

Human genetic information is stored in the 46 chromosomes contained in the cell nucleus. In humans (and most other terrestrial organisms) the genetic information is encoded in the nucleic acid DNA (deoxyribonucleic acid). The DNA occur as a double-stranded molecule in the shape of a double helix, that is to say the two molecules are wound together around a common axis. Each strand consists of a long chain of chemicals called nucleotides. These nucleotides are made up of four different nitrogenous bases: adenine (A), thymine (T), cytosine (C), and guanine (G).



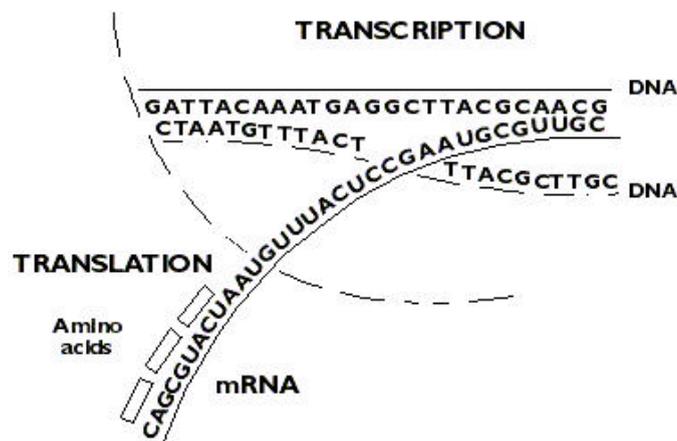
Contained in the nucleus of each human cell are 23 pairs of chromosomes comprising all of the human genome. Each chromosome consists of tightly coiled threads of DNA. Each DNA molecule contains many genes. A gene is a specific sequence of nucleotide bases that carry the information required for constructing proteins.

These are the “letters” in the genetic alphabet. The linear order of the four bases constitutes the genetic information. A set of three nucleotides, called codon,

corresponds to an amino acid. Thus, for example, TTT codes for the amino acid phenylalaline, whilst CAG codes for glutamine. This relationship between a codon and an amino acid is called the genetic code and has been known since the 1960s. A gene is a sequence of DNA that specifies one particular protein. A gene that describes how a protein consisting of, e.g., 200 amino acids should be synthesized is thus corresponded by a DNA sequence of 600 bases. The sequence of the codons along the DNA determines the order between the amino acids in a protein. An individual protein can vary in length from a hundred to more than a thousand amino acids.⁴ Correspondingly the length of a gene (i.e. the number of nucleotides) might vary dramatically.

The entire genome contains about three billion base pairs divided between the 46 chromosomes. However, only about 2-3% of the DNA are coding regions, exons.⁵ The rest, introns, or non-coding regions have no established function.⁶ These non-coding regions are situated both inside and in between the genes. Because of the presence of introns, genes are generally ten times longer than is needed to code for proteins.⁷ The length of a DNA molecule is thus considerable. In fact, DNA molecules are among the largest molecules known.⁸ The total DNA in one cell is several meters long when stretched out. It has been estimated that if all the DNA in a human were stretched out, it would extend from the earth to the sun and back again.⁹

The instructions for protein synthesis in the DNA are transmitted with the help of another nucleic acid, RNA (ribonucleic acid). The RNA copies the DNA message through the creation of a messenger RNA (mRNA), a process known as transcription. The mRNA is a molecule similar to a single strand of DNA. The mRNA is thus a complementary cast of the DNA that carries the genetic code to the site of protein synthesis. However, it is only the exons, or the coding regions of the gene, that is transcribed into the mRNA.



When genes are expressed, the genetic information of the DNA molecule is transcribed to a messenger RNA. This process is similar to DNA replication

⁴ Brändén, p. 18.

⁵ Brändén, p. 101.

⁶ However, it is known that part of these DNA sequences act as “operating regions” capable of turning genes on and off, thus directing the expression of the gene.

⁷ Nationalencyclopædien, Vol. 7, p. 378.

⁸ Department of Energy, Primer on Molecular Genetics, p. 9.

⁹ Britannica Macropaedia, Vol. 19, p. 710.

(described below). The mRNA molecule then leaves the cell nucleus and associates with ribosomes to make the amino acids specified by the codons.

There exist twenty different amino acids. If one single nucleotide coded for an amino acid, only four amino acids could be specified. If two nucleotides were needed to specify an amino acid, then 16 different amino acids could be constructed. Although with a combination of three different bases, 64 different codons are possible, which is more than necessary. This is referred to as the redundancy (or degeneracy) of the genetic code.¹⁰ Thus some amino acids correspond to more than one triplet of nucleotides. As an example, the codons GCA, GCC, GCG and GCT are all alternative codes for the amino acid alanine.

		Second Position of Codon									
		T		C		A		G			
First Position of Codon	T	TTT	Phe	TCT	Ser	TAT	Tyr	TGT	Cys	Third Position of Codon	T
		TTC	Phe	TCC	Ser	TAC	Tyr	TGC	Cys		C
		TTA	Leu	TCA	Ser	TAA	Ter	TGA	Ter		A
		TTG	Leu	TCG	Ser	TAG	Ter	TGG	Trp		G
	C	CTT	Leu	CCT	Pro	CAT	His	CGT	Arg	T	
		CTC	Leu	CCC	Pro	CAC	His	CGC	Arg	C	
		CTA	Leu	CCA	Pro	CAA	Gln	CGA	Arg	A	
		CTG	Leu	CCG	Pro	CAG	Gln	CGG	Arg	G	
	A	ATT	Ile	ACT	Thr	AAT	Asn	AGT	Ser	T	
		ATC	Ile	ACC	Thr	AAC	Asn	AGC	Ser	C	
		ATA	Ile	ACA	Thr	AAA	Lys	AGA	Arg	A	
		ATG	Met	ACG	Thr	AAG	Lys	AGG	Arg	G	
	G	GTT	Val	GCT	Ala	GAT	Asp	GGT	Gly	T	
		GTC	Val	GCC	Ala	GAC	Asp	GGC	Gly	C	
		GTA	Val	GCA	Ala	GAA	Glu	GGA	Gly	A	
		GTG	Val	GCG	Ala	GAG	Glu	GGG	Gly	G	

A sequence of three nucleotides is a codon and a codon encodes for an amino acid. However, with 64 different combinations possible for producing only 20 different amino acids, there is some redundancy. When more than one codon codes for the same amino acid the codons are referred to as degenerate codons. Each gene commences with a “start-triplet” (usually ATG) and finishes with a triplet that signals the end of the gene (one of the codons TGA, TAG or TAA).

Thus, when a DNA sequence is known, the amino acid sequence can readily be generated. However, the opposite is not true due to the degeneracy of the genetic

¹⁰ Brändén, p. 20.

code. I.e. when the amino acid sequence is known, one cannot with certainty deduce the DNA sequence.

2.2.2 DNA replication

The other important function of the DNA molecule, to transfer the genetic information to the following generations, is inherent in its ability to create a precise replication of itself. Each time a cell divides into two daughter cells, its full genome is duplicated. This is due to its double-stranded nature and to the fact that against each nucleotide on one strand corresponds to a complementary nucleotide on the other strand. Thus the nucleotide A in one strand always corresponds to the nucleotide T in the other strand. Similarly G always pair with C. A pair of two nucleotides held together by a weak bond is called a base pair. This complementary character means that one strand can be looked upon as a negative print of the other, which is used to create a new (positive) copy. This mechanism is called replication. The bonds between the base pairs break and the two strands of the DNA molecule unwind. Each strand then acts as a template for the formation of a new strand, creating a new DNA molecule, which is an exact copy of the original DNA molecule. When free nucleotides are present in the medium surrounding the DNA they might pair with the complementary bases of the single strands of DNA, binding together with the help of enzymes. Thus two new DNA molecules are created, each with one old and one new strand.

2.3 Recombinant DNA Technology

Being inseparable from DNA patenting, one of the most important techniques in biotechnology is the recombinant DNA technology, which can be described as the controlled joining of DNA from different organisms. Actually the term includes a variety of molecular maneuvers, including cleaving and recombining fragments of DNA, inserting DNA into bacteria so that large quantities of genetic material can be produced and determining the nucleotide sequence of a DNA segment.¹¹ Gene cloning is a means of producing large amounts of copies of genes, using bacteria. To perform gene cloning, specific enzymes are used as “biological scissors” cutting DNA sequences containing the genes of interest. Once the gene has been removed from the donor cell, it is inserted into the bacterial cell, using a vector¹². Through the rapid reproduction of bacteria, large amounts of the desired gene can quickly be produced.¹³ The host cell or organism may then express the human DNA sequence, producing the desired proteins encoded by the cloned genes.

Traditionally, genes were identified and cloned through a method of working “backwards”. Starting with isolating a protein with a useful biological property from

¹¹ Britannica Macropaedia, Vol 19, p. 716.

¹² A vector is a DNA molecule with an ability to transfer itself between different hosts. Plasmids, i.e. small, circular DNA molecules found in certain bacteria, are often used as vectors

¹³ Britannica Macropaedia, Vol 19, p. 716.

an organism, this protein is then processed to determine its amino acid sequence. Then the codons that can code for some of the amino acids are determined, using the genetic code. A probe can then synthetically be manufactured from the nucleotides hence found. Because some amino acids have several possible codons it might be necessary to design a set of probes that covers all possible codons for the amino acid sequence.¹⁴ To isolate a specific gene a DNA-library is used. A library is a collection of recombinant DNA molecules containing the whole human genome created through cloning. The probe produced to locate the gene is labeled with a radioisotope and hence mixed with the library. The probe will then hybridize to the segment of the DNA, which has a sequence complementary to its own. Through the help of the radioisotope, it is possible to isolate the gene which encodes the useful protein.¹⁵ However, this approach was both time-consuming and expensive. In the beginning of the 1990's a new approach for identifying genes was developed. This method is known as complimentary DNA (cDNA) sequencing. This method is taking advantage of the fact that cells know which parts of the DNA are genes. The cell copies the protein-encoding parts of the DNA into mRNA in the transcription phase. By isolating the mRNA molecule and treating it with enzymes, the mRNA forms a cDNA molecule by "reverse transcription". The cDNA is then processed to determine its nucleotide sequence. Since the mRNA is a copy only of the protein encoding sections of the genomic DNA, the cDNA obtained is a purified "artificial" gene.¹⁶ However, even cDNA sequencing has its drawbacks. The traditional approach identified and isolated a gene encoding a known protein with a known function. The cDNA obtained with the new approach often encodes an unknown protein with an unknown function. Thus, cDNA-sequencing paints only a fraction of the picture compared to that of the traditional approach.

2.4 The use of DNA in biotechnology

Biotechnology is used in several ways. To treat diseases recombinant DNA technique can be used to produce a biologically active molecule that have certain therapeutic uses, such as proteins. These proteins can be used in the development of pharmaceuticals. Genetically engineered vaccines have also been produced.¹⁷ DNA sequences are further useful for diagnosing certain genetic diseases, such as cystic fibrosis. Therapeutic biotechnology can also be used to repair fundamental genetic errors.¹⁸ To treat patients suffering from genetic diseases, it is possible to insert the "correct" gene into the cell to replace the one that is defective (somatic gene therapy). In this way the affected cells would themselves produce the protein, allowing the person to function normally.¹⁹ The advantage of producing pharmaceuticals with the help of human genes are that they are products of a constant raw material and that they have the same composition as the body's own counterpart²⁰, which minimizes the risk of allergic reactions. Yet another use of

¹⁴ Borson, 35 IDEA 1995:4, p. 466.

¹⁵ Britannica Macropaedia Vol. 19, p. 716.

¹⁶ Borson, 35 IDEA 1995:4, p. 465.

¹⁷ Swain, p. 36.

¹⁸ Borson, 35 IDEA 1995:4, p. 463.

¹⁹ Borson, 35 IDEA 1994:4, p. 463.

²⁰ Nationalencyclopedia, Vol. 7, p. 399.

biotechnology is by inserting human DNA into animals, making them produce useful substances, for example in their milk.

2.5 The Human Genome Project and The Human Genome Organization

The Human Genome Project (HGP), initiated by the US Congress in 1988 and formally begun in 1990, is an international effort to map all the twenty-three pairs of chromosomes within the human genome. Originally conceived as a 15-year project, rapid technological advances have accelerated the project to an expected completion date of 2003. The goals are to discover all of the estimated 100 000 genes (the human genome) and make them accessible for further biological study. Another objective is to determine the complete sequence of the 3 billion base pairs. By January 1999, over 7600 genes had been mapped to particular chromosomes and an estimated 10% of the DNA had been sequenced. It is important to notice, however, that this does not involve immediate understanding of the genes. A full comprehension of the functions of the genes lies outside the project and will require a lot more research. Detailed DNA information is however key to further studies of the human genome. Other goals are to store the information found in databases, to develop tools for data analysis and to address the ethical, legal and social issues that may arise from the project.²¹ Most of the research is done in the US, Europe and Japan, with the US bearing the largest share of the budget, contributing 303 million dollars in 1998.

The Human Genome Organisation (HUGO) is an international organization of scientists involved in the human genome project. HUGO was established in 1989 to promote international collaboration within the project. HUGO fosters the exchange of data and encourages the spreading and sharing of technologies as well as promoting consideration of ethical, legal, social and intellectual property issues surrounding the project.²²

2.6 Conclusions

For the past two decades, there has been an explosion of innovative growth in the field of biotechnology. The use of recombinant DNA technology has revolutionized the development of new drugs. Traditionally, drugs were either natural products or synthesized chemical substances. Today an increasing number of pharmaceuticals are produced using biotechnological processes. By using recombinant DNA technology, limitations of supply can be overcome to produce large quantities of useful proteins. In addition, drugs manufactured using this technology are to a greater extent free from contamination by impurities, having less potential for causing adverse effects. Moreover, the discoveries made through the Human Genome Project have further increased the knowledge and the potential of the human

²¹ Information about the Human Genome Project can be found at:

www.ornl.gov/hgmis/home.html

www.er.doe.gov/production/ober/helsrd_top.html

www.nhgri.nih.gov/HGP

²² Information about the Human Genome Organisation can be found at www.gene.ucl.ac.uk/hugo.

genes, creating a surge of research and development. In short, biotechnology is one of the most expansive industries today.

3. PATENTS

3.1 The implications of holding a patent

The object of holding a patent might be described as the right of the inventor, for a limited period of time, to prevent others from commercially making, using and selling his invention. It can therefore be characterized as a negative right in the sense that the inventor does not need the patent to exploit his invention but without the patent others can copy and profit by it.²³ Sometimes it is described as a contract between the society and the inventor, allowing the inventor to get a sort of monopoly on the invention in exchange for disclosing the invention, allowing others to take part of useful information. Thus, a patent secures a privileged market opportunity for the holder of the patent.²⁴ Different theories for the justification of the patent system exist. Freidrich-Karl Beier has developed a modern interpretation of the widely accepted “patent theories” put forth in the fifties by Fritz Machlup. According to these theories we grant patents to recognize the intellectual property of the inventor; to reward the inventor for his useful services; to encourage inventors and industry to invent, invest and innovate; and to further the early disclosure and wide dissemination of technical knowledge.²⁵

3.2 The research exemption

Many patent systems allow for research exemption, or experimental use exemption, of a patented invention. Such a use is deemed not to be an infringing act provided that the research is not aimed at commercialization of a product.²⁶ In the US this exemption is mainly recognized through court decisions²⁷, whereas other countries often have an explicit exemption included in the text of the statute.²⁸ However it is difficult to discern the scope of this exemption with any precision, as it is the definition of this exemption that often cause problems.²⁹ There is also a tendency of case law to interpret the research exemptions narrowly.³⁰

²³ Swain, p. 12.

²⁴ Straus, in Vogel and Grunwald (eds.), p. 13.

²⁵ Beier, 11 IIC 1980:5, p. 563.

²⁶ Swain, p. 30.

²⁷ Eisenberg, Patenting Research Tools and the Law, p. 4-5.

Found at www.nap.edu/readingroom/books/property/2.html#chap2

²⁸ See, for example, Japanese Patent Act Sec. 69; Section 11 Paragraph 2 of the German Patentgesetz; The UK Patens Act Section 60 (5) and Article L.613-5 of the French Code de la Propriété Intellectuelle.

²⁹ Swain, p. 30.

³⁰ Straus, in Vogel and Grunwald (eds.), p. 13 n. 5.

3.3 The different patent systems

3.3.1 USA

In the US the patent rules are laid down in the federal law. The starting point for any discussion of federal law in the United States is the United States Constitution. The federal government has only those powers provided in the constitution. The legislative powers are outlined in Article 1, Section 8, which comprises 18 clauses. Clause 8 is devoted to protection of inventions; it reads: “[The Congress shall have Power...] To promote the Progress of Science and useful Arts, by securing for limited Times to...Inventors the exclusive Right to their respective...Discoveries.” The current patent statute was enacted in 1952 and is contained in Title 35 of the United States Code.³¹

The most common type of patent, called utility patent, covers new and useful inventions that meet certain requirements. Utility patents are uniformly meant when “patent” is used alone and confers a twenty-year protection. Plant patents reward discovery of any new variety of plants. The last category of patent is the design, which protect ornamental features of articles of manufacture.³²

The US patent system is based on a “first-to-invent” basis. This means that the person who was the first to make an invention is entitled to a patent. The United States is one of few countries to have such a system. Even though this system is seen to be fairer to inventors by assuring that the patent holder genuinely is the first person to come up with the invention, the legal ambiguities this can create can lead to expensive processes to establish the paternity of inventions.³³ US law further allows the applicant to take advantage of a grace period of one year before the filing date which can be used for pre-publication and pre-use. This principle might be advantageous for scientists who have a need for early publication of their research for career advancement.³⁴ One drawback is, however, that most countries don’t accept this principle and therefore don’t grant patents for inventions disclosed under such a grace period. Another difference is the question of transparency. In the US, unlike Japan and Europe, applications are not published and the first document to be published is the granted patent.³⁵ Since the examination process may take several years, experimental and other detail can be hidden from competitors for a long time.³⁶ Another implication is that it is impossible to know if a certain patent was applied for if a patent never was granted³⁷, thus hindering others to take part of the information in order to improve the invention.

If the PTO examiner determines that the invention does not meet the patentability criteria, the applicant may seek to revise the decision by appealing to the Board of Appeals and Interferences. If the application again is rejected, the applicant may seek

³¹ Nies, 21 IIC 1990:4, p. 482-483.

³² Jones, Overview of United States Patent law, p. 1, found at www2.ari.net/foley/patentov.html.

³³ Masood, 397 Nature 1999, p. 457.

³⁴ Swain, p. 36-37. See also Grunwald, in Vogel and Grunwald (eds.), p. 101.

³⁵ Swain, p. 17.

³⁶ Masood, 397 Nature 1999, p. 457.

³⁷ Patent på biotekniska uppfinningar, Gentekniknämndens utredningsserie, p. 12.

review in Court. The Board's decision may be appealed directly to the US Court of Appeals for the Federal Circuit (the CAFC). Alternatively, the decision may be appealed to the District Court of Columbia and then appeal that decision to the Federal Circuit.³⁸ Appeals from decisions of the CAFC are taken to the United States Supreme Court. However, an appeal to the Supreme Court is discretionary and not a matter of right. In the US there is no postgrant opposition division, which exists both in Japan and in Europe. Thus an opposing third party may only challenge a patent in litigation through court.³⁹

In all countries, once a patent is granted, it is out of the jurisdiction of the patent offices. Matters of infringement, the scope of the patent, or any other questions that arise out of the grant are within the jurisdiction of the courts.

3.3.2 European Patent Convention

The European Patent Convention (EPC) of 1973 established the so-called European patent. The main objects of the EPC, as set out in its preamble, are "to strengthen co-operation between the States of Europe in respect of the protection of inventions" and "that such protection may be obtained in those States by a single procedure for the grant of patents and by the establishment of certain standard rules governing patents so granted." Applicants who wish to obtain national patents in Member States can make an application under the EPC to the European Patent Office (EPO).⁴⁰ Thus, the EPC provides for a centralized examination of patent applications. Once granted, it results in the grant of national patents in those Member States that were designated by the applicant. The applicant thus obtains what is often called a "bundle" of national patents in the designated states.⁴¹

The European system is a "first-to file" system, meaning the inventor who is first to file for an application has priority. "First-to-file" has become standard outside the US since it is less complicated and costs less to process than applications based on the "first-to-invent" principle.⁴² Under the EPC there is no grace period; non-prejudicial disclosures up to six months before the filing date are only accepted in certain exceptional cases, which are specified in Article 55.⁴³ On the other hand are European patent applications published 18 months after the filing date. This requirement serves the important function of making the information contained in the patent application available to the public at an early stage, providing third parties with an instrument to improve the invention.

³⁸ Nies, 21 IIC 1990:4, p. 483.

³⁹ Swain, p. 63.

⁴⁰ Currently the following countries have signed the EPC: Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Liechtenstein, Luxembourg, Monaco, Netherlands, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

⁴¹ Paterson, p. 3.

⁴² Masood, 397 Nature 1999, p. 457.

⁴³ Evident abuse in relation to the applicant or a display of the invention at a limited number of selected exhibitions.

The EPO has five first instance departments: the Receiving Section, the Search Division, the Examining Division, the Opposition Division and the Legal Division. The Examining Division is responsible for the substantive examination of the application, as to whether the application and invention meet the requirements. If a patent is granted, any person may, within nine months of the grant, file an opposition to the Opposition Division, which will examine the complaint. If a party is “adversely affected” by a decision of a first instance department, he may appeal to one of the Boards of Appeal. Article 106 EPC provides that every decision issued by one of the first departments may be appealed to a Board of Appeal.⁴⁴ The Boards of Appeals are the second and final instances within the EPO. If an application is refused or if a patent is revoked by a decision of a Board of Appeal, no further appeal is possible either within or outside the EPO, and such decision is therefore final.⁴⁵ Once a European patent is granted, it has the effect of a national patent granted by a Contracting State. Issues of validity and infringement are thus matters for national law and national courts.⁴⁶

3.3.3 The European Union Directive

In July 1998 the Directive on the Legal Protection of Biotechnological Inventions finally came into force. This directive has had a troubled history. The original proposal to harmonize the patenting of biotechnological inventions was made as far back as 1985.⁴⁷ An original draft was published in 1988 but after considerable debate it was rejected by the European Parliament in 1995. The Commission introduced the second draft in December 1995, after amending certain provisions specifically designed to address ethical and environmental issues. The directive seeks to clarify and harmonize biotechnology patent practice in Europe. The aim of the directive was to introduce in the Member States of the European Union a comparable level of protection to biotechnological inventions conferred in the US and Japan.⁴⁸ Although biotechnology inventions had already been granted by European patent offices (either at a national level or by the EPO) there still existed a lack of harmonization and hence uncertainty about the patentability of some inventions.⁴⁹ Where the patent laws of Japan and the US as well as the EPC are silent as far as genes are concerned, the EU directive contains specific articles concerning the patenting of human genes. However, the directive does not add any new type of patent practice. The rules of national patent law remain the essential basis for the legal protection of biotechnological inventions.⁵⁰ However, by clarifying the scope of protection available and ensuring that different standards of patentability are not applied, one seeks to encourage investment in the field of biotechnology.⁵¹ The Member States are obliged to implement the directive into the national legal systems before July 30

⁴⁴ There are several Technical Boards of Appeal (TBA), each covering a differing subject field in the examination of the patent appeal. There is also a Legal Board of Appeal, however this is not concerned with the refusal or grant of a European patent.

⁴⁵ Paterson, p. 4.

⁴⁶ Article 64 (3).

⁴⁷ Nott, EIPR, 1998:9, p. 347.

⁴⁸ Straus, 26 IIC 1995:6, p. 942.

⁴⁹ EuropaBio, found at www.europa-bio.be/publications/patent02.htm.

⁵⁰ Recital 8 of the Directive.

⁵¹ Recital 3 of the Directive.

2000. The European Patent Office is not bound directly by the Directive, but the administrative side of the EPO is currently working towards a supplement to the Implementing Regulations to correspond with the directive.⁵²

3.3.4 Japan

Like Europe, Japan operates under the “first-to-file” principle.⁵³ When it comes to the requirement of pre-application disclosures, Japan strikes a medium between the US and the EPC. The applicant may conduct public experiments with the invention prior to filing a patent application. Furthermore, he may disclose the invention in a printed publication or present a written description of the invention to a scientific body designated by the JPO. Finally, the invention may be publicly displayed by the applicant at certain types of exhibitions. All these exceptions require however that the applicant must file a patent application within six months of the earliest of these acts.⁵⁴ The applicant files the application at the Japanese Patent Office (JPO). Since 1990 the JPO has a fully operational electronic filing system and it is recommended that the applications are filed online. If the examiner finds that the claimed invention fails to meet the requirements for patentability, a notice of rejection will be sent to the applicant, giving him an opportunity to respond to the rejection.⁵⁵ If the application is finally rejected, the applicant may demand a trial within 30 days.⁵⁶ If an amendment is filed together with the request for appeal, the examiner must reconsider the grounds for rejection in light of the new amendment before an appellate board inspects the appeal. The trial is conducted by a collegial body of three or five trial examiners.⁵⁷ The examining procedure and appeals might take several years but in any event the application is published eighteen months after the filing date.⁵⁸ If a patent is granted, a disagreeing third party is allowed to oppose the grant within 6 months of the publication of the patent.⁵⁹ Any litigation concerning the grant of the patent comes under the jurisdiction of the Tokyo High Court.⁶⁰

3.4 Requirements for patentability

To receive a patent, there are certain requirements that must be met. The claimed invention must be of patentable subject matter in addition to meeting three threshold standards, namely novelty, nonobviousness (usually referred to as inventive step in Europe and Japan) and utility (industrial applicability in Europe and Japan).

⁵² Oser, 30 IIC 1999:1, p. 2 n. 10. See also Jaenichen, News on Biotech in the European Patent Office and on Infringement Cases in its Contracting States, p. 2, found at www.jaenichen.com/news.htm.

⁵³ Japanese Patent Act Sec. 39.

⁵⁴ Japanese Patent Act Sec. 30.

⁵⁵ Japanese Patent Act Sec. 49 – 50.

⁵⁶ Japanese Patent Act Sec. 121.

⁵⁷ Japanese Patent Act Sec. 136 (1).

⁵⁸ Japanese Patent Act Sec. 64.

⁵⁹ Japanese Patent Act Sec. 113 - § 120.

⁶⁰ Japanese Patent Act Sec. 178 (1).

Furthermore, the application must contain a description of the invention together with one or several claims, defining the scope of protection sought.

3.4.1 Patentable subject matter

During the Uruguay Round in 1993 an Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs) was negotiated, which set up certain conditions for intellectual property protection. The TRIPs agreement involves more than a hundred countries, covering industrial countries as well as the developing world. This agreement can be seen as an attempt to impose the same high standards of protection in the developing countries as in the industrialized countries. This is an issue that has become increasingly important due to the growing global trade. Since patents are limited to the territories where they have been granted, it is necessary to file patent application in each country where patent protection is needed.⁶¹ Article 27 (1), concerning patentable subject matter, requires the parties of the agreement to inaugurate the ability to seek protection for *any* inventions in *all* fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. This wide scope of patent-eligible subject matter is illustrated in the US Supreme Court decision *Diamond v. Chakrabarty*⁶², which repeated the intention of the US Congress to allow “anything under the sun that is made by man” to be patentable.⁶³

3.4.2 What is not patentable

There are several creations that are not considered to be an invention and therefore not patentable. This can be something abstract such as a disembodied idea or a simple disclosure resulting from the mere use of one’s observational and analytical skills. Among things in this category are discoveries, scientific theories and mathematical methods. Another group is not patentable due to its non-technical character, such as aestetelical creations and presentation of information. In the US, the PTO and the Courts developed a “natural products” doctrine, claiming that “patents cannot issue for the discovery of the phenomena of nature. They are manifestations of laws of nature, free to all men and reserved exclusively to none. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end.”⁶⁴

As biotechnology inventions are frequently utilized in medical therapy or diagnostic methods, it should be mentioned that therapeutical or surgical treatments as well as diagnostic methods practiced on the human body are not considered inventions capable of being patented under the EPC or the Japanese Patent Act.⁶⁵ It should be understood, however, that substances or compositions for use in such methods can be

⁶¹ Swain, p. 19.

⁶² *Diamond v. Chakrabarty*, 447 US 303, 206 USPQ 193 (1980).

⁶³ *Diamond v. Chakrabarty*, 447 US at 309.

⁶⁴ *Funk Bros. Seed Co v. Kalo Inoculant Co.*, 333 US 127 (at 130), 76 USPQ 280 (1948).

⁶⁵ EPC Art. 52 (4); JPO’s Implementing Guidelines for examination of Industrially Applicable Inventions, section 2.1.

protected. In the US there is no counterpart to this regulation, meaning that the US PTO will issue patents for methods of treatment.

3.4.3 Novelty

The requirement of novelty stipulates that an invention must not form part of the state of the art, which is the sum of publicly known technology.⁶⁶ Thus the first step is to determine what forms part of the state of the art. The second step is to determine whether the subject matter claimed in the patent application differs from this prior art.⁶⁷

In Europe objective and absolute novelty is required, that is to say the invention should be new to the inventor but must also be new to everyone else, i.e. it must not be previously disclosed in any manner at the filing date of the application.⁶⁸ According to EPC Article 54 (2):

“The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application.”

However, in the US absolute novelty is not required, due to the grace period mentioned earlier. 35 USC § 102 states:

“A person shall be entitled to a patent unless
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States
...”

Subparagraph (a) here refers to the “first inventor” requirement whereas subparagraph (b) refers to the grace period. The one-year grace period in the US only applies to printed publications or patents anywhere in the world and to public uses or sales within the US.⁶⁹ A seminar at a scientific congress does not trigger the grace period.⁷⁰ As we have seen, Japan has a six-month grace period that is limited in scope as to the extent of the activities excused. Apart from these exemptions (outlined above at 3.3.4), a patent will be denied if the invention was publicly known in Japan, publicly worked in Japan or described in a publication distributed anywhere in the world prior to the filing date of the application.⁷¹

⁶⁶ Jones, p. 4.

⁶⁷ Paterson, p 133.

⁶⁸ However, the Paris Convention allows the inventor 12 months to prepare foreign patent applications for filing after the initial patent application. Thus it allows the inventor to claim the date of the first application as the priority date of the invention.

⁶⁹ Jaenichen, p. 192 n. 78.

⁷⁰ Jaenichen, p. 192 n. 79.

⁷¹ Japanese Patent Act Sec. 29 (1).

A claimed invention lacks novelty unless it includes at least one essential technical feature that distinguishes it from the prior art.⁷² For lack of novelty to be found, all the technical features of the claimed invention in combination must have been communicated to the public.⁷³ The information on which an objection of lack of novelty is based must thus be derived from one document only.⁷⁴ If the technical features of the invention are not directly and unambiguously disclosed in combination, then the invention has not previously been made and is novel.⁷⁵ Furthermore, novelty must be substantive and not simply a matter of language.⁷⁶

3.4.4 Nonobviousness/Inventive Step

Determination of whether a claimed invention involves an inventive step takes place if it has been established that the combination of claimed technical features is not part of the prior art, and that the claimed invention therefore is novel.⁷⁷ Since novelty can easily be obtained by adding only insignificant modifications to the state of the art, a more demanding requirement is needed to secure that only innovations with a certain substance are granted a patent.⁷⁸ Nonobviousness is often the most problematic material condition for patentability. While the first step for determining the inventive step is the same as for the assessment of novelty, i.e. what forms part of the state of the art, the second step is here to determine whether the claimed subject matter was or was not obvious to a person skilled in the art.⁷⁹ Where the novelty requirement asks whether an invention is disclosed in one document in the prior art, the nonobviousness requirement asks whether the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.⁸⁰

According to the “Guidelines for Examination in the European Patent Office” the term “obvious” means that which does not go beyond the normal progress of technology but merely follows plainly or logically from the prior art. That is to say something that does not involve the exercise of any skill or ability beyond what is to be expected from a person skilled in the art.⁸¹ The invention should normally be considered as a whole. It is therefore not sufficient to draw the conclusion that a claimed invention is obvious merely because individual parts of the claim taken separately are known or might be found to be obvious.⁸²

⁷² Paterson, p. 139.

⁷³ Paterson, p. 139.

⁷⁴ However, if there were explicit references to another document, this shall also be taken into consideration.

⁷⁵ Foerster, p. 3, found at www2.ari.net/foley/foerster.html.

⁷⁶ Paterson, p. 142.

⁷⁷ Paterson, p. 150.

⁷⁸ Ducor, 75 JPTOS 1995:11, p. 876.

⁷⁹ Paterson, p. 133.

⁸⁰ The requirements for inventive step in Europe, US and Japan are expressed in EPC Article 56, 35 USC § 103 and the Japanese Patent Act Sec. 29 (2) respectively.

⁸¹ Guidelines for Examination in the European Patent Office C-IV 9.3.

⁸² Guidelines for Examination in the European Patent Office C-IV 9.6.

In the EPO, the assessment of inventive step is usually done with a “problem and solution” approach, involving three stages.⁸³ The starting point of this assessment is to determine the closest prior art. This is usually that which discloses a technical effect or a use similar to that of the invention and which has the minimum of structural or functional difference from what is claimed in the invention.⁸⁴ Secondly the objective technical problem to be solved in progressing from the closest prior art to the claimed invention is determined. The technical problem is the task of modifying the closest prior art to provide the technical effects that the invention provides over the closest prior art.⁸⁵ The technical problem may be to improve in some way an effect already known from the prior art or it may be to make available a totally new effect.⁸⁶ Finally the obviousness is assessed. This poses the question whether a person skilled in the art⁸⁷, faced with the technical problem and knowing the prior art, would arrive at something within the invention. The US PTO does not require a problem-solution approach. Instead US Courts have traditionally applied a four-tier analysis of nonobviousness: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the pertinent art; and (4) secondary considerations such as commercial success, long felt but unresolved needs and failure of others.⁸⁸ These secondary considerations were developed in the case *Graham v. John Deere Co.*⁸⁹ and they have also been recognized by the EPO in a number of cases.⁹⁰ The invention should not be rejected as unpatentable just because it was “obvious to try”. However, for something to be considered as obvious, it does not require the absolute predictability of success but merely a reasonable expectation of success.⁹¹

3.4.5 Utility/Industrially applicable

Paragraph 101 of the US Patent Act provides that “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 therefor.” Article 57 EPC is often considered to be the European counterpart of the utility requirement under US patent law. It simply 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.”⁹² With some differences these two requirements are essentially the same. The interpretations of these regulations are very wide. According to the Guidelines of the EPO, “industry” should be understood in a broad sense, including any activity of technical character. This is meant to be an activity that belongs to the useful or practical arts as distinct from the aesthetic arts.⁹³ In the US, words often

⁸³ Guidelines for examination in the European Patent Office, C-IV 9.5.

⁸⁴ Leonard, p. 3, found at www2.ari.net/foley/leonard.html.

⁸⁵ Leonard, p 3.

⁸⁶ Leonard, p. 3.

⁸⁷ The obviousness is determined with respect to the nature of the skilled person and the common general knowledge amongst persons skilled in the particular art.

⁸⁸ Jaenichen, p. 227 n. 98.

⁸⁹ *Graham v. John Deere Co.*, 383 US 1, 148 USPQ 459 (1966).

⁹⁰ Paterson, p. 158-159.

⁹¹ Richards and Cord, 71 Patent World 1995 April, p 29. See also Jaenichen p. 227 and 232.

⁹² Under Japanese Patent Act, the requirement for industrial applicability is expressed in Sec. 29 (1).

⁹³ Guidelines for the Examination in the European Patent Office, C-IV 4.1.

repeated are the intention of the Congress to allow “anything under the sun that is made by man” to be patentable.⁹⁴

In the US, the patent applicant must show that the invention serves a practical purpose as well as being operable or capable of use. In the case of *Brenner v. Manson*⁹⁵, the US Supreme Court rejected the overly broad scope of utility that traditionally had been applied. Instead it set the stage for the modern judicial interpretation of the utility provision. The Court pointed out that merely producing something that may be the object of scientific research was insufficient to justify the grant of a patent. In short, the Court stated that utility must be definite and in currently available form, not merely for further investigation or research.⁹⁶

It can be argued that industrial applicability is a more focused test for patentability than that of utility, which need not be industrial. However, the notion of mere “susceptibility”, i.e. capability rather than proven actuality, might be used to admit inventions whose industrial applicability is potential and perhaps entirely speculative. Nonetheless, since the EPO requires the invention to be a solution to a problem, an entirely speculative piece of research will probably not stand up to this.⁹⁷ Hence, this may level out the possible differences between the notion of industrial applicability and that of utility. It should be noted that the utility requirement is primarily concerned with the ability of the invention to achieve its stated purpose and should not be equated with commercial utility. The patent application must identify the utility of the invention and describe how it is to be used but there is no need to show any commercial potentials of the invention. The invention is patentable even if it requires further development before it can be put on the market.⁹⁸

3.4.6 Disclosure requirements

A further requirement for patentability is the obligation for the inventor to give a sufficiently detailed description of the invention in the patent application to enable others in the relevant field of art to make and to use the invention without undue experimentation.⁹⁹ Thus, the disclosure must be clear enough for the invention to be reproduced by a person skilled in the art, taking into account the common general knowledge in the art. In other words, the written description must make it apparent that the applicant has indeed invented the subject matter claimed.¹⁰⁰ The disclosure requirement is expressed in 35 USC § 112, EPC Article 83 and the Japanese Patent Law § 36 (3) and (4). In the US the application must also disclose the best mode known to the inventor, at the time the patent application was filed, for carrying out the invention.¹⁰¹ Under the EPC, there is no “best mode” requirement, as made clear

⁹⁴ *Diamond v. Chakrabarty*, 447 U.S. at 309.

⁹⁵ *Brenner v. Manson*, 383 US 519 (1966), 148 USPQ 689 (1966).

⁹⁶ Richards and Cord, 71 Patent World 1995 April, p. 25.

⁹⁷ Crespi, EIPR 1995:9, p. 437.

⁹⁸ Crespi, 11 Trends in Biotechnology 1993:10, p. 407.

⁹⁹ In the US, a distinction is made between “written description”, which should describe the invention itself, and “enabling disclosure”, which should describe how to make and use the invention.

¹⁰⁰ Hoffert, 12 The Scientist 1998, p. 2.

See also www.the-scientist.library.upenn.edu/yr1998/july/hoffert_p1_980706.html

¹⁰¹ 35 USC § 112.

in the Erythropoietin/Amgen case.¹⁰² The description should be supplemented by making a deposit of materials, e.g. genes, that are not reproducible from a written description alone.¹⁰³ Current patent practice applies the deposit regulations originally developed in respect of microorganisms directly or analogously to DNA sequences.

3.4.7 The Claim

Every application for patent must include a claim, which is the precise legal definition of what the patent applicant asserts has been invented. The claim defines the outer periphery of protection sought by the applicant. The wording of the claims are thus very important, as they define whatever scope the inventor considers to be warranted. The claims in a patent application must logically follow what is disclosed in the written description.¹⁰⁴ However, the claims are not technical descriptions of the disclosed invention, but a legal document.

3.5 Conclusions

No matter where patent protection is being sought, the three basic requirements novelty, inventive step (nonobviousness) and industrial applicability (utility) must be met. These requirements are thus essentially the same within the European, American and Japanese patent systems. The TRIPs agreement has further diminished the differences that exist between the different systems. This is of importance to large international corporations who hold multiple patents in the different regions. None of the three patent systems contain any express reference to the patenting of human genes. However, the European Union recently adopted the Directive on the legal protection of biotechnological inventions. This directive does not imply a new kind of patent protection, but is merely designed to harmonize and clarify the patent regulations in the different member states.

4. PATENTING THE HUMAN GENOME

There is nothing unusual nowadays about patenting genes. Patents based on DNA have been granted by patent offices in the industrially developed countries for more than 15 years.¹⁰⁵ The specific case law on biotechnological inventions have over the last decade developed to the point where important principles have been established and clear trends have become discernible. The US is traditionally one of the major markets for biotechnology and therefore many of the standards set there are of interest to the biotechnology industry in the rest of the world. In this chapter I will

¹⁰² T 412/93, Erythropoietin/Amgen, EP-B1 148 605, section 76.

¹⁰³ Straus, in Vogel and Grunwald (eds.), p. 14. See e.g. Article 13 (1) of the Directive on the Legal Protection on Biotechnological Inventions.

¹⁰⁴ Swain, p. 12.

¹⁰⁵ Marshall, 275 Science 1997, p. 780.

address the issue of the patenting of genes and other parts of the DNA by going through the requirements for patentability in each case.

4.1 The development towards the patenting of genes

The notion that a gene can be patented was established in 1980, when the US Supreme Court held that Anada Chakrabarty, a molecular biologist working for General Electric, could patent a genetically engineered organism. Chakrabarty had created a new bacterium containing cDNA sequences not normally found in the same organism, making it capable of breaking down crude oil. No bacteria present in nature possessed such traits and Chakrabarty therefore sought patent protection. The US PTO initially rejected the patent application on the grounds that microorganisms are products of nature and, as living things, not patentable. The Supreme Court, however, held in its decision *Diamond v. Chakrabarty*¹⁰⁶ that the micro-organism, although living, was a product of human ingenuity and hence patentable. Arguing that the Congress deliberately had used such expansive terms as “manufacture” and “composition of matter” to give patent laws a wide scope, the court ruled that the claim was not to a natural phenomenon but to a nonnaturally occurring manufacture or composition of matter. This opened up the possibility for exceptions to the “natural products” doctrine established in *Funk Bros.* for materials that, although existing in nature, are not naturally present in a form that is “useful”.¹⁰⁷ Later decisions made it clear that even “normal” DNA sequences are considered artificial products and therefore patentable.¹⁰⁸ In applying the patentability requirements, DNA sequences have been characterized as chemical compounds. Decisions in this field had made clear that patents could be issued on claims to naturally occurring chemicals, such as adrenaline and acetylsalicylic acid, as long as they were purified.¹⁰⁹ With this background, it cannot be considered as farfetched to allow patents on other naturally occurring substances, such as genes. A study, published in 1996, revealed that between 1981 and 1995 patent offices in the United States, Europe and Japan had issued 1175 patents on human DNA sequences.¹¹⁰

4.2 The gene as an invention

Generally, patent systems do not differentiate amongst inventions according to their origin. Thus, a gene, cell or protein of human origin is evaluated in the same way as other inventions. But because gene sequences exist naturally, some argue that it is impossible for such matter to be invented, they can only be discovered. As we have seen, discoveries alone are not patentable because they do not advance the useful arts. It is how the discovery is applied that turns it from a mere discovery into a constructive contribution to technology worthy of protection as an invention.¹¹¹

¹⁰⁶ *Diamond v. Chakrabarty* 447 US 303, 206 USPQ 193 (1980).

¹⁰⁷ Borson, 35 IDEA 1995:4, p. 468.

¹⁰⁸ Marshall, 275 Science 1997, p. 781.

¹⁰⁹ Eisenberg, 15 Nature Genetics 1997, p. 125-126.

¹¹⁰ Thomas et al., 380 Nature 1996, p. 387.

¹¹¹ Holmes, Patent World, Aug 1998, p. 17.

Thus, for something to be characterized as an invention it must involve a technical solution to a technical problem. The key rests in the fact that a naturally occurring substance must be extracted from its natural state; it must be the subject of some manipulation to be novel, nonobvious and of patentable utility. To find a substance freely occurring in nature is a mere discovery and therefore unpatentable. However, if a substance, e.g. a DNA sequence, found in nature has been isolated from its surroundings and if it can be properly characterized by its structure or by other parameters, then the sequence per se may be patentable.¹¹² In the US, purified products, e.g. genes, are generally patented as “compositions of matter”.

4.2.1 Novelty

Another aspect of the argumentation against patenting genes is that, because of its pre-existence in nature, the gene cannot satisfy the novelty requirement. But the test for novelty does not focus on the question of pre-existence of what is claimed.¹¹³ Even though DNA sequences exist in nature, they are not necessarily part of the state of the art, which means accessible to the public.¹¹⁴ The patentability lies thus in the fact that the gene is put at the society’s disposal for the first time.¹¹⁵ The policy seems to be to treat human gene sequences like chemical substances, and in accordance with the legal practice in the field of chemical products, a substance is considered novel if it is isolated for the first time.¹¹⁶ In the words of the EU directive “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.”¹¹⁷ As we have seen, a mere discovery of a gene sequence is not a patentable invention. On the other hand might a discovery be the starting point for the development of an invention, i.e. the practical application of a discovery may be patented. In the case of a gene, it is necessary to identify where the gene coding for a specific useful protein is located in the human genome and then to isolate and decode the gene.¹¹⁸ The contribution to the art lies in making the gene available in a form that can be used to produce e.g. a pharmaceutical product.¹¹⁹ The novelty arises because the technical processes used to identify, purify and classify the element and to reproduce it outside the human body are man-made and cannot be accomplished by nature alone.¹²⁰

Furthermore, the cDNA obtained through recombinant DNA techniques is not a true copy of the original natural genomic DNA, since the non-coding regions of the gene are removed during transcription. The cDNA is thus a purified version of the gene, containing only those sequences that code for proteins. It must also be recognized

¹¹² Guidelines for examination in the European Patent Office, C-IV 2.3. See also the Directive on the legal Protection of Biotechnological Inventions, Article 5 (2).

¹¹³ Crespi, EIPR 1995:9, p. 432.

¹¹⁴ Galloux, in Knoppers (ed.), p. 364.

¹¹⁵ Koktvedgaard, NIR 1994:4, p. 441.

¹¹⁶ Galloux, in Knoppers (ed.), p. 364.

¹¹⁷ Directive on the legal protection of biotechnological inventions, Article 3.2.

¹¹⁸ Teschemacher, NIR 1994:1, p. 52.

¹¹⁹ Crespi, EIPR 1995:9, p. 432.

¹²⁰ Directive on the legal protection of biotechnological inventions, Recital 21.

that cDNA molecules as such do not exist in nature.¹²¹ In one of the most important cases concerning the patenting of genes in Europe, Howard Floney Institute/Relaxin¹²², the Opposition Division of the EPO held that the claimed DNA sequences were cDNAs, which do not occur in the human body and hence the sequences claimed were novel for this reason alone.¹²³ Moreover, they stated, even if the claims had included the genomic DNA sequences, they would have been novel since the existence of the form of relaxin claimed was unknown before the gene sequences were isolated by the inventor. The Opposition Division referred to the Guidelines¹²⁴ and stated that “It is established patent practice to recognise novelty for a natural substance which has been isolated for the first time and which has no previously recognised existence.”¹²⁵ Furthermore, in the Alpha-interferons-case¹²⁶ and the Erythropoietin-case¹²⁷, the Technical Board of Appeal held that a genomic DNA library does not destroy the novelty of a DNA sequence contained therein if there is no probe for identifying the DNA sequence. The argument was that the library did not make the claimed DNA sequences sufficiently accessible to the public to be part of the state of the art. Another decision points out that the same is true for cDNA sequences, i.e. that a cDNA library does not anticipate a particular cDNA contained in the library if there is no suitable probe.¹²⁸

4.2.2 Nonobviousness

Obviousness rejections of claims to DNA generally fall in one of two categories. A claimed DNA sequence might be rejected over a known DNA sequence, which codes for the same protein. A claimed DNA sequence might also be rejected over a known amino acid sequence, which the claimed DNA encodes.¹²⁹ Normally a claimed DNA encoding a specific protein would be rendered *prima facie* obvious over prior art disclosing a DNA sequence which codes for the same protein, on the ground of structural similarity between the two DNA sequences.¹³⁰ However, when the obtained DNA has advantageous effects that a person skilled in the art cannot foresee in comparison with other genes having a different base sequence, the invention of the newly obtained gene is not obvious.¹³¹ Thus, the DNA claimed can be rendered nonobvious on its various properties and characteristics beyond that of a mere information transfer vehicle, even if it is structurally similar to a DNA disclosed in the prior art.¹³² This is because degenerate codons can be selected for their ability to increase expression in a given host. Although different codons encode for the same

¹²¹ Crespi, EIPR 1995:9, p. 433.

¹²² Relaxin, EP-B1 112 149, OJ EPO 1995, 388.

¹²³ Relaxin, EP-B1 112 149, OJ RPO 1995, 388. Section 4.2 of the decision.

¹²⁴ Guidelines for examination in the European Patent Office, C-IV 2.3.

¹²⁵ Relaxin, EP-B1 112 149, OJ RPO 1995, 388. Section 4.3.1 of the decision.

¹²⁶ T 301/87, Alpha-interferons/Biogen, EP-B 32 134, OJ EPO 1990, 335.

¹²⁷ T 412/93, Erythropoietin/Amgen, EP-B1 148 605.

¹²⁸ Jaenichen, p. 202.

¹²⁹ Bozicevic, 74 JPTOS 1992:10, p. 752.

¹³⁰ Bozicevic, 74 JPTOS 1992:10, p. 753.

¹³¹ Trilateral Project 24.1 – Biotechnology, p. 24 under 2.3 Inventive Step (2).

¹³² Bozicevic, 74 JPTOS 1992:10, p. 753.

amino acid, certain hosts “prefer” specific codons, giving an increased efficiency in the production of the protein.¹³³

The second category is concerned with whether a DNA sequence would be considered nonobvious if the corresponding amino acid sequence is known in the prior art. In the area of biotechnology, obviousness has been a tricky question since scientists use similar techniques to isolate different gene sequences, even though the gene sequence may be new. It has been suggested that DNA technology is now so routine as to make obvious certain inventions that 10 years ago were considered nonobvious.¹³⁴

In the US two court decisions on the issue whether or not knowledge of the amino acid sequence of a protein, in conjunction with a reference indicating a general method of isolation, renders the gene encoding the known protein *prima facie* obvious¹³⁵ have attracted much attention. One important decision in this area was that of the Federal Circuit in the case of *In re Bell*.¹³⁶ In *Bell*, the Court held that two newly retrieved DNA sequences were non-obvious from their corresponding amino acids, known in the prior art, regardless of retrieval method. *Bell* claimed the natural DNA sequences which codes for human insulin-like growth factors I and II. Both the amino acid sequences and a general method for isolating a gene were known in the prior art. The US PTO examiner determined that it would have been obvious “albeit tedious” to prepare probes to obtain the claimed DNA molecules. The Board of Appeals affirmed that a case of *prima facie* obviousness had been established despite the lack of conventional indicia of obviousness, e.g. structural similarity between the DNA and the amino acid sequence. The Board reasoned that although a protein and its DNA are not structurally similar in the conventional sense, they are correspondingly linked via the genetic code. A person skilled in the art could thus have cloned the DNA sequences without undue burden. The Court reversed the PTO’s decision, holding that a *prima facie* case of obviousness had not been established. Knowing the structure of the protein, the genetic code can indeed be used to hypothesize possible structures for the corresponding gene. But because the protein sequence disclosed in the prior art consisted of amino acids that are encoded by several codons, the Court held that, due to this degeneracy of the genetic code, there were a large number of nucleotide sequences that might code for the protein in question.¹³⁷ Therefore, given the nearly infinite number of possibilities suggested in the prior art, the claimed sequences could not have been obvious.¹³⁸ Nor did the prior art teaching a method of isolating a gene render the claimed DNA sequence obvious, since it in fact appeared to teach away from the claimed invention by stating that it was counterproductive to use a probe having more than 14-16 nucleotides where *Bell*

¹³³ Bozicevic, 74 JPTOS 1992:10, p. 755.

¹³⁴ Borson, 35 IDEA 1994:4, p. 473.

¹³⁵ The notion of “*prima facie* obviousness” is a procedural tool, used to revert the burden of proof to the applicant. The PTO bears the initial burden of proof in establishing a case of *prima facie* obviousness. If *prima facie* obviousness is established, the applicant can dispute this with convincing evidence showing otherwise. A *prima facie* case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art.

¹³⁶ *In re Bell*, 991 F.2d 781, 26 USPQ 2d 1529 (Fed. Cir. 1993)

¹³⁷ In fact it has been calculated that an averagely sized protein can be encoded by 10^{36} different DNA sequences.

¹³⁸ *In re Bell*, 991 F.2d at 784.

used a probe of 23 nucleotides.¹³⁹ The Court concluded by remarking that the PTO's focus on Bell's method was misplaced. "Bell does not claim a method. Bell claims compositions, and the issue is the obviousness of the claimed compositions, not of the method by which they are made."¹⁴⁰ However, in other cases the deduction from the corresponding DNA sequence from a known amino acid sequence might be relatively straightforward. Thus, if a person skilled in the art would have a reasonable expectation of success in obtaining the DNA sequence, then the DNA sequence would be rendered *prima facie* obvious.¹⁴¹

A similar case in the assessment of obviousness is the decision of CAFC in *In re Deuel*.¹⁴² Again it was a question of whether or not knowledge of the amino acid sequence, in combination with a reference indicating a general method of isolating the gene, rendered the invention, i.e. the gene, *prima facie* obvious. Two of the claims were directed to specifically disclosed cDNA molecules, whereas another two claims encompassed all isolated DNA sequences encoding a particular protein. These claims were thus not limited to specific DNA sequences, as in *Bell*. However, the application did not describe the chemical structure of, or taught how to obtain the DNA, except the two disclosed cDNA molecules. A partial amino acid of the protein was disclosed in the prior art combined with a general technique for isolating a gene. The PTO rejected the application. It stated that when the sequence of a protein is placed in the public domain, the gene is also placed in the public domain because of the routine nature of cloning techniques. The Court reversed the PTO's decision. Starting with the issue of *prima facie* obviousness, the Court explained that a case of *prima facie* obviousness is normally based upon structural similarity, i.e. an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. But because proteins are structurally different from DNA, the Court held that proteins cannot suggest DNA.¹⁴³ The Court then went on to explain that because of the redundancy of the genetic code the two disclosed cDNAs could not have been contemplated by a person skilled in the art. Again it held that a prior art disclosure of the amino acid sequence only permits one to hypothesize an enormous number of DNA sequences coding for the protein. No particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate that it should be prepared. Only a general motivation to search for some gene that exists does not necessarily make obvious a specifically defined gene.¹⁴⁴ However, the Court recognized that a different result might pertain if the protein disclosed in the prior art had been sufficiently small and simple, so to render each possible DNA obvious over the protein. Next the Court reaffirmed its finding in *Bell*, again stating that the PTO's focus on the method for isolating the claimed DNA molecules was misplaced since the claims defined compounds, not methods. The Court admitted, however, that an enabling process taught in the prior art was a factor to be taken into consideration when determining patentability. But, it stated, there must still be prior art that suggests the claimed compound in order for a *prima facie* case of obviousness to be

¹³⁹ *In re Bell*, 991 F.2d at 784.

¹⁴⁰ *In re Bell*, 991 F.2d at 785.

¹⁴¹ *Maebius*, 76 JPTOS 1994:6, p. 508-509.

¹⁴² *In re Deuel*, 51 F.3d 1552, 34 USPQ 2d 1210 (Fed. Cir. 1995).

¹⁴³ *In re Deuel*, 51 F.3d at 1558.

¹⁴⁴ *In re Deuel*, 51 F.3d at 1558.

made out. Concluding that the fact that one can conceive a general process in advance for preparing an undefined compound does not mean that a claimed specific compound was precisely envisioned and therefore obvious. The two specified cDNA molecules were therefore held to be nonobvious.¹⁴⁵ Moving to the generic claims to any DNA encoding a specific protein, the Court stated that they might have been obvious if the complete amino acid sequence of the protein had been disclosed in the prior art. This information might have enabled a person skilled in the art to envision the idea of, and, with the aid of a computer, identify all possible DNA sequences of the protein in question. But disclosed in the prior art was only a partial amino acid sequence and therefore the claimed genus was not obvious.¹⁴⁶ Thus, the CAFC strongly reaffirmed, and indeed broadened, the underlying message of Bell.

The Deuel decision was welcomed by the biotechnology industry, which had been worried by the PTO's strict interpretation of the nonobviousness criterion. However, the decision has also been criticized on the grounds that the Court stretched the nonobviousness standard to the point it becomes indistinguishable from novelty, creating a per se rule of patentability for newly retrieved DNA sequences.¹⁴⁷ According to these cases, the nonobviousness criterion appears to direct itself not to the level of inventive skill needed to obtain the sequence, but to the absence of structurally similar DNA molecules in the prior art. This does not fit with the perception among research scientists of what constitutes scientific achievement.¹⁴⁸ Thus, it has been held that the use of the structural similarity criterion leads to the wrong results. In the field of chemistry it is indeed a useful test of prima facie obviousness, since analogs in this field provide suggestion to make a new product.¹⁴⁹ However, when it comes to DNA it can be argued that structural similarity should not be the general test. In the case of DNA, the test of structural similarity has a limited value, since the value of DNA lies in the information encoded in its sequence. The informational identity between the protein and the DNA sequence encoding it should be as relevant as the structural similarity in the test for obviousness.¹⁵⁰ Thus, a disclosure in the prior art of an amino acid sequence should be able to render the DNA sequence obvious, since the protein can suggest the DNA sequence to a person skilled in the art. The statement of the Court that it only is possible to hypothesize a large number of possible DNA sequences from an amino acid sequence and that a specific DNA sequence therefore is nonobvious, was held to be superficial. While it is true that knowledge of a protein sequence does not give a direct and immediate conception of the corresponding DNA, it is not true that a DNA cannot possibly be conceived from its corresponding protein sequence. All it takes are some routine hybridization procedures.¹⁵¹ Obviousness does not require that the new invention can be conceived without the slightest experimentation. All obviousness requires is a reasonable expectation of success. Finally, the Court's opinion that the method of isolation is largely irrelevant to the question of obviousness has also been attacked. The argument is that the product and the process are two aspects of the same phenomenon and that the method by which a product

¹⁴⁵ In re Deuel, 51 F.3d at 1559.

¹⁴⁶ In re Deuel, 51 F.3d at 1560.

¹⁴⁷ Ducor, 77 JPTOS 1995:11, p. 872.

¹⁴⁸ Eisenberg, 15 Nature Biotechnology 1997, p. 126.

¹⁴⁹ Ducor, 77 JPTOS 1995:11, p. 884.

¹⁵⁰ Ducor, 77 JPTOS 1995:11, p. 873.

¹⁵¹ Ducor, 77 JPTOS 1995:11, p. 888.

was made is fundamental in determining whether the invention was or was not suggested to a person skilled in the art.¹⁵²

The situation was somewhat clarified in *Ex parte Goldgaber*.¹⁵³ On a first glance, the PTO seems to decide contrary to the Federal Circuit's decisions, claiming that the method by which a compound is made is a relevant factor in evaluating the obviousness of a compound. In *Goldgaber*, the Board of Appeals found that the applicants claim directed to a DNA sequence encoding the Alzheimer's beta-amyloid protein unpatentable in view of prior art, which disclosed the sequence of the protein and further described degenerate nucleotide probes which could be used to isolate the gene. The Board's decision was due to the specificity with which the prior art disclosed specific probes which could be used in the isolation of the gene. The Board decided that the prior art was more "comprehensive" than that cited in the earlier cases, which only disclosed a general method of isolating genes in the prior art. The Board expressly rejected the idea that a per se rule of nonobviousness could be inferred from *Bell and Deuel*. The decision indicates that the PTO does not consider an examiner to be precluded from considering prior art teaching a method for isolating a gene, which creates a reasonable expectation of success, in the determination of obviousness of a DNA molecule.¹⁵⁴

In the Trilateral Project, the three Patent Offices considered the question of whether a partial amino acid sequence of a protein disclosed in the prior art would render a DNA sequence encoding the protein in question obvious.¹⁵⁵ The US PTO answered that no per se rules of obviousness exist and that each application must be examined with a fact-specific analysis of the claims presented compared to the prior art.¹⁵⁶ The EPO held that such a DNA sequence would be considered obvious, since it is a common procedure for a person skilled in the art to isolate the DNA sequence when a partial amino acid sequence is known.¹⁵⁷ The JPO gave a similar answer, but concluded that if the isolation of the entire DNA sequence is a difficult task, or if the effect achieved by the specific DNA isolated is unexpectedly superior, the DNA would not be held obvious.¹⁵⁸

4.2.3 Utility

There has not been much debate surrounding the requirement of utility when it comes to the patenting of complete gene sequences. Utility is normally a low hurdle for biotechnological inventions to overcome. As we have seen, there are several possible uses for genes. However, in order to comply with the utility criterion it is necessary to disclose the function of the gene, its practical purpose, as envisaged in *Brenner v. Manson*, discussed above. This is true also in Europe and Japan.

¹⁵² *Ducor*, 77 JPTOS 1995:11, p. 892.

¹⁵³ *Ex parte Goldgaber*, 41 USPQ 2d 1172.

¹⁵⁴ Miles, *Modern Trends in Intellectual Property*, p. 3-4, under I B and C.

Found at www.law.uiuc.edu/ipls/www/mtip/crm.html

¹⁵⁵ www.jpo-miti.go.jp/saikine/contents.htm

¹⁵⁶ www.jpo-miti.go.jp/saikine/uspto/u63.htm

¹⁵⁷ www.jpo-miti.go.jp/saikine/epo/e63.htm

¹⁵⁸ www.jpo-miti.go.jp/saikine/jpo/j63.htm

According to JPO's Implementing Guidelines, the gene cannot be considered an industrially applicable invention if the utility of that gene is not specified.¹⁵⁹ Thus, in the case of a gene encoding a protein, it is not enough to know that the gene codes for a certain protein, the function of the protein must also be disclosed.¹⁶⁰

In the case of *In re Brana*¹⁶¹, the CAFC ruled on what patent applicants for pharmaceutical inventions have to prove regarding practical utility. Brana had claimed certain pharmaceutical compounds for use as antitumor agents. The PTO had rejected the applicant's claims on the ground that the tests used to determine the utility of the compounds were not sufficient to establish a reasonable expectation that the compounds had practical utility. The CAFC thought otherwise. Noting that the initial burden was on the PTO to challenge the assertion of utility, the Court reversed PTO's decision. The Court added that even if the PTO had met this *prima facie* burden, the evidence that the applicant submitted was sufficient to rebut the rejection. It further held that the requirement of utility to obtain patent protection must not be confused with the requirement for obtaining government approval to market a particular drug for human consumption. FDA approval "is not a prerequisite for finding a compound useful within the meaning of the patent laws [...] Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development."¹⁶²

The criticism of the US PTO handling of patent applications that had surfaced due to several cases where the CAFC had reversed the PTO's decision, led the PTO to review the guidelines for examining patent applications. On July 14, 1995 the US PTO issued new guidelines for utility examination.¹⁶³ In reviewing an application for patent protection, the examiner should determine if the applicant has asserted any utility for the claimed invention. If these assertions would be considered credible by a person skilled in the art, in view of the evidence disclosed, then a rejection based on utility is not to be made. If the applicant asserts that the claimed invention is useful for treating a human and this utility is credible, the examiner should not require that the applicant demonstrate that the therapeutic agent is safe or fully effective. However, the applicant has to provide a reasonable correlation between the activity and the asserted use. The burden is on the examiner to support the case for rejection, which must be properly grounded on evidence. To support a *prima facie* showing of no utility, there must be established that it is more likely than not that a person of ordinary skill in the art would not consider credible the asserted utility of the claimed invention.¹⁶⁴ The new guidelines thus have the effect of reducing the burden on applicants, relaxing the standard of utility.

¹⁵⁹ Implementing Guidelines for Inventions in Specific Fields, Chapter 2 Biological Inventions, section 1.3.1.

¹⁶⁰ Directive on the legal protection of biotechnological inventions, Recital 24.

¹⁶¹ *In re Brana*, 51 F.3d 1560, 34 USPQ 2d 1436 (Fed. Cir. 1995).

¹⁶² *In re Brana*, 51 F.3d at 1568.

¹⁶³ 60 Fed. Reg. 36263.

¹⁶⁴ Ladas & Parry November 1995 Information Letter, found at www.ladas.com/bulletins/1995/bulletin.1195.US1.html.

4.2.4 Disclosure requirements

Several cases in the US have dealt with the question of what kind of information that must be disclosed in the application of a biotechnological invention in order to satisfy the written description requirement. In the case of *Amgen v. Chugai Pharmaceuticals*¹⁶⁵, Amgen had claimed all the analogs of the gene encoding erythropoietin, a protein which stimulates the production of red blood cells. It was hence determined that the number of claimed DNA was potentially enormous. However, details for preparing only a few of the analog genes were disclosed. The Court held that it was well established that a patent applicant is entitled to claim his invention generically, however this implies that he has to disclose the invention appropriately. It is necessary that the inventor provide a disclosure sufficient to enable someone skilled in the art to carry out the invention. For a claim to analog DNA sequences, that means disclosing how to make and use enough sequences to justify grant of the claims sought.¹⁶⁶ A person skilled in the art could not have determined which other genes that encoded erythropoietin analogs since Amgen only had described how to prepare a few of the analog genes. The Court therefore concluded that the claims were broader than the enabling disclosure and the claims were thus held to be invalid.

*Fiers v. Revel*¹⁶⁷ concerned three inventors who claimed priority for inventions involving the DNA encoding human fibroblast beta-interferon, a protein that promotes viral resistance in human tissue. Revel was denied priority because of the absence of the actual sequence of the DNA in the disclosure document. The Court stated “ An adequate description of a DNA requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it; what is required is a description of the DNA itself...A bare reference to a DNA with a statement that it can be obtained by reverse transcription is not a description; it does not indicate that Revel was in possession of the DNA.”¹⁶⁸ It further held that the description required a precise definition, such as by structure, formula, chemical name, or physical properties.

One of the most bitterly fought infringement cases in the US is the case of *Regents of the University of California v. Eli Lilly*.¹⁶⁹ The patents in suit related to recombinant plasmids and microorganisms that produce human insulin, a protein involved in the regulation of sugar metabolism. The CAFC held that the Regents’ claims were invalid for failure to provide an adequate written description. First, the Court considered a claim to a microorganism containing a human insulin cDNA. However, the disclosure did not provide a description of the cDNA in question but only a general method for obtaining it and a description of the amino acid sequences that it encodes. The Court repeated the words from *Fiers v. Revel* that an adequate written description of a DNA requires a precise definition of that DNA, e.g. by disclosing the structure of the DNA. Describing a method of preparing a cDNA or even describing

¹⁶⁵ *Amgen v. Chugai Pharmaceutical*, 927 F.2d 1200, 18 USPQ 2d 1016 (Fed. Cir. 1991).

¹⁶⁶ *Amgen v. Chugai Pharmaceutical*, 927 F.2d at 1213.

¹⁶⁷ *Fiers v. Revel*, 984 F.2d 1164, 25 USPQ 2d 1601 (Fed. Cir. 1993)

¹⁶⁸ *Fiers v. Revel*, 984 F.2d at 1170-1171.

¹⁶⁹ *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 25 USPQ 2d 1398 (Fed. Cir. 1995).

the protein that the cDNA encode, does not necessarily describe the cDNA itself.¹⁷⁰ Then the Court went on to consider claims which concerned generically recited cDNA's of "a vertebrate". However, the UC had only described a rat insulin-encoding DNA. The Court held that a description of a species does not necessarily constitute a description of a genus of which it is a part. To sufficiently describe a genus, one must reveal some features that distinguish genes falling into that genus from others. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.¹⁷¹ The Court concluded that a "description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to the members of the genus, which constitute a substantial portion of the genus."¹⁷²

Several cases from the EPO indicate that the situation is different in Europe. According to Jaenichen, the EPO takes a more pragmatic approach when assessing enabling disclosure, providing a larger scope of protection.¹⁷³ Studying EPO decisions, it can be concluded that it might be sufficient to characterize the invention by its function. Under the EPO practice, as different from the requirements in the US, structural predictability is not necessary for acknowledging enabling disclosure.¹⁷⁴ When a group of compounds is claimed, a single example usually provides sufficient support. In the case of Polypeptide Expression/Genentech¹⁷⁵, the TBA concluded that an invention is sufficiently disclosed if at least one way of carrying out the invention is clearly indicated, enabling the person skilled in the art to obtain the invention. Even if some variants of a functionally defined component are unspecified, the disclosure requirement is met if certain suitable variants are disclosed. The disclosure doesn't need to include specific instructions as to how every possible variant within the functional definition should be obtained. In the case of Alpha-Interferons/Biogen¹⁷⁶, the TBA stated that: "Variations in the constitution of a class of genetic precursors, such as recombinant DNA molecules, claimed by a combination of structural limitations and functional tests are immaterial to the sufficiency of the disclosure provided the skilled person could obtain reliably members of the class without necessarily knowing in advance which member would be made available."

However, some recent developments might indicate a change of direction of the EPO. In the Hepatitis B/Biogen¹⁷⁷ case, the TBA went on to grant a patent with broad claims. Sticking to its usual stance it held that the lack of data on how to produce a compound of analogous function did not mean that the disclosure was deficient of relevant technical information necessary for reproducing the claimed invention in practice. Shortly after this decision, another case, Fuel Oils/Exxon¹⁷⁸,

¹⁷⁰ Eli Lilly, 119 F.3d at 1567.

¹⁷¹ Eli Lilly, 119 F.3d at 1568.

¹⁷² Eli Lilly, 119 F.3d at 1569.

¹⁷³ Jaenichen, p. 143 and 234. However, since the scope of patent protection does not derive solely from the literal breadth of the claims, but also from the doctrine of equivalents, the final scope of protection conferred to a US and European patent might be highly similar. Jaenichen, p. 143.

¹⁷⁴ Jaenichen, p. 235.

¹⁷⁵ T 292/85 Polypeptide Expression/Genentech, OJ EPO 1989, 275.

¹⁷⁶ T-301/87 Alpha-Interferons/Biogen. EP-B 32 134, OJ EPO 1990, 335.

¹⁷⁷ T-886/91 Hepatitis B/Biogen EP-B1 13 828.

¹⁷⁸ T-409/91 Fuels Oil/Exxon, OJ EPO 1994, 653.

was decided in which the Board came to a conclusion contradiction the earlier decisions. In this case the Board held that the application must contain sufficient information so as to allow a person skilled in the art to carry out the invention within the *whole* area that is claimed. In an infringement case in Britain concerning the patent granted by the EPO relating to Hepatitis B, the British Court of Appeal came to a different conclusion than the TBA. The British court made extensive quotes from the Fuel Oil/Exxon decision and established that the sufficiency of the disclosure requirement cannot be determined without having regard to the width and character of the claims. The court held the claims in the Hepatitis B patent invalid, stating that the disclosure must be detailed enough so as to enable a person skilled in the art to perform the claimed invention across its full width and not just by reference to certain variants. A patent applicant has a choice of how wide to draw the claims. If he chooses to draw the claims widely, he must also make a correspondingly wide disclosure. If the applicant is unable to make such a disclosure, it shows that he is seeking to claim an invention to which he is not entitled. The standards applied by the British court are thus very similar to those applied by the CAFC in its decisions relating to sufficiency of disclosure. Some subsequent decisions by some Boards of Appeal testify that there might now be less discrepancy between the principles applied in national courts and the EPO, since the recent EPO decisions show a more stringent approach towards the disclosure requirement.¹⁷⁹ It must be said that, having regard to the far-reaching effects of a product patent, and to the fact that the *quid pro quo* for granting a patent is the disclosure of the invention, stricter rules as to the sufficiency of disclosure must be seen as desired.¹⁸⁰ The general test should be that a person skilled in the art should be able to reproduce the invention from the description in the disclosure document.

Also the JPO allows generic claims to DNA sequences. However, in the Implementing Guidelines it is specified that if “a large amount of trials and errors or complicated experimentations are needed to produce those genes beyond the reasonable extent that can be expected from a person skilled in the art” the enablement requirement is not met.¹⁸¹

4.3 Patenting ESTs

Contrary to what one might think, the patenting of full-length genes has led a relatively quiet life. The real controversy didn't start until 1991, when the US National Institutes of Health (NIH) applied for patent protection of several thousand partial cDNA sequences, so-called expressed sequence tags (ESTs). An EST is part of a sequence from a cDNA clone. Thus, an EST is a fragment of a full-length gene. It is usually between 150 and 400 nucleotides in length.¹⁸²

¹⁷⁹ Straus, 26 IIC 1995:6, p. 942.

¹⁸⁰ Straus, 26 IIC 1995:6, p. 947-948.

¹⁸¹ Implementing Guidelines for Inventions in Specific Fields, Chapter 2 Biological Inventions, section 1.1.2.1.1 (2) (1).

¹⁸² Gugerell, in Vogel and Grunwald (eds.), p. 110.

4.3.1 *The EST saga*

In the early days of the Human Genome Project, scientists had mapped and sequenced only about 5% of all genes.¹⁸³ It appeared that reading the rest would take many years. However, Craig Venter, a Human Genome Project investigator working at NIH, changed that. Venter developed a method to rapidly find and sequence parts of the human genome. He refined the technology to locate protein-encoding DNA sequences that was developed through the 1970s and 80s. Instead of working backward from a protein which is already known, as is done in traditional DNA research, Venter isolated the mRNA molecule, which only contains the protein-encoding regions of the DNA. From this mRNA, a cDNA copy can be obtained. However, to speed up the process further, only parts of the cDNA molecule are produced.¹⁸⁴ These parts of the cDNA gene are called expressed sequence tags.

Figuring the sequences had value that should be protected, the NIH filed patent applications in 1991 and 1992¹⁸⁵, claiming a total of 6869 ESTs.¹⁸⁶ Shortly thereafter, the UK Medical Research Council followed suit. This sparked a fierce debate. As long as genes were being discovered slowly, protein by protein, using the traditional biotechnological approach, the question of patenting the human genome was not predominant in the public debate. However, with the possibility of the entire genome being sequenced rapidly, with only a few institutions profiting from it, the controversy took on new dimensions.¹⁸⁷ The problem was that the applications included claims not only to the ESTs themselves, but also to the entire gene corresponding to each EST, as well as the protein coded for by that gene. An EST is sufficiently unique to be part of only one complete cDNA gene, and therefore can be used to identify the corresponding full-length gene. Thus, the theory behind the claims is that the full-length gene is “inherent” within the sequence of the fragment.¹⁸⁸ However, the function of these genes was not known, i.e. the proteins they encode were unknown or at least of unidentified function.

In August 1992, the US PTO issued a preliminary rejection of the NIH’s patent claims, based primarily on lack of utility due to lack of known demonstrated uses. The NIH decided in 1994 not to appeal and the application was abandoned.¹⁸⁹ However, several commercial companies had by now decided to prosecute similar claims. The controversy surrounding ESTs has many different aspects. Many scientists feared that the patenting of ESTs would disrupt the flow of information

¹⁸³ Carey et al., *Business week*, May 22 1995, p. 37.

¹⁸⁴ This is because the mRNA molecule is very fragile and breaks easily.

¹⁸⁵ Then-NIH Director Bernadine Healy believed this to be in the best interest of the public, encouraging the rapid development of products for disease treatment. The idea was to license the ESTs to industry, making it more likely that useful products would be developed. The argument was that private investors would be unwilling to commit necessary capital to the development of these inventions unless they have exclusive patent licenses to protect their profit margins. For two different views on the NIH patent filings, see Adler 257 *Science* 1992, p. 908 and Eisenberg, 257 *Science* 1992, p. 903.

¹⁸⁶ Anderson, 263 *Science* 1994, p. 904.

¹⁸⁷ Borson, 35 *IDEA* 1994:4, p. 476.

¹⁸⁸ Borson, 35 *IDEA* 1994:4, p. 481. See also Eisenberg 257 *Science* 1992, p. 904.

¹⁸⁹ This decision was due to the new director of NIH, Harold Varmus, who justified the decision to abandon the application based on his belief that patents on ESTs are not in the best interests of the public or science. Anderson, 263 *Science* 1994, p. 909. In the light of this the UK MRC also withdrew its patent applications.

within the international Human Genome Project, greatly increasing project costs.¹⁹⁰ Another concern is that a patent on an EST may block-off the future patenting of the full-length gene, decreasing interest to identify and isolate the corresponding full-length gene.

¹⁹⁰ Suiter and Wax, 67 Patent World November 1994, p. 16.

4.3.3 The HUGO Statement

In 1995, HUGO issued a statement on the patenting of DNA sequences.¹⁹¹ It stated that HUGO was concerned that the patenting of partial and uncharacterized cDNA sequences (i.e. ESTs) would reward those who made routine discoveries but penalize those who determine biological function or application. In the statement they made clear that the scientific work involved in generating ESTs is a useful but straightforward extension of a technique that had been in use on a smaller scale for years. The sequencing of any gene necessarily involves the sequencing of individual small fragments. However, the process from an EST to a full-length cDNA or genomic DNA is not straightforward. Using a partial gene sequence to find the entire gene is an important research activity that requires skill and innovation. Furthermore, it was held that the task of identifying biological functions of a gene is by far the most important step both in terms of its difficulty and its social benefit. This step therefore merits the most incentive and protection. In conclusion, they hold that even if technological advances have rapidly increased the speed of sequencing the DNA, this remains the easy part. Other steps in biological discovery, such as the understanding and the use of genes and gene products, remain challenging. Offering broad patent rights to those who undertake massive but routine sequencing efforts – whether for ESTs or for whole genes – while granting more limited rights or no rights to those who make the far more difficult and significant discovery of the genes' biological functions would be unfortunate.

The main concern is thus that companies that resort to only read the nucleotide sequence of the genome, and don't care to identify the biological function of that sequence, may obtain valuable patent rights whereas companies that have invested significant resources in the identification of the function of the gene may find themselves blocked by such patents. In other words, HUGO considered it improper for manufacturers of ESTs to control product development when their contribution to the advancement of science is minimal. The scope of protection granted by patents should not extend beyond the achievement of the inventor to include inventions yet to be made by others.

4.3.4 The situation in the US

When it comes to the patentability requirements, the main discussion point has been that of utility. Most ESTs encode only small parts of proteins; meaning that even though the EST codes for amino acids, the protein is incomplete and its function is often unknown.¹⁹² Claiming only the EST as a protein encoding sequence would hence generally be rejected on the ground of lack of utility. The same is true if the application also claimed the corresponding gene if the function of this gene is not

¹⁹¹ The HUGO Statement on the patenting of DNA Sequences can be found at www.gene.ucl.ac.uk/hugo/patent.htm

¹⁹² Borson, 35 IDEA 1994:4, p. 480.

disclosed in the application, as seen above. To overcome the utility hurdle, applicants therefore listed other possible uses for ESTs, such as use in forensic identification.¹⁹³

However, the main value of ESTs lies in its use as chromosome markers. Since an EST has a long enough sequence to be specific for the particular gene from which it originate, the EST will bind to the exact gene on the chromosome for which it has a complimentary sequence when it is added to a DNA library. ESTs may therefore be used as probes to isolate and obtain the full coding region of their corresponding genes.¹⁹⁴ But according to the doctrine in *Brenner v. Manson*, the utility requirement in the US is not satisfied if the invention simply is part of ongoing research. The ESTs may be viewed as intermediates useful in a process of isolating genes. But if the full-length gene is of unknown function, a patent claiming an EST for the object of obtaining the corresponding gene would be exactly the kind of speculative utility rejected in *Manson*.¹⁹⁵ However, in light of the new utility examination guidelines, the use of ESTs as probes appears to satisfy the standard of “credible utility”. Instead of the substantial utility required in *Brenner*, the new guidelines accepts any reasonable use that the applicant has identified that can provide a public benefit. A claim that an EST can be used as a probe would probably be considered credible under the PTO guidelines.¹⁹⁶ Nonetheless, this lowering of the standard of utility has been met by critique. One argument is that patents on ESTs are part of a trend moving towards the filing of a new patent application for every step taken in biotechnological research. This would lead to patents on inventions with “minimal marginal utility” over the preceding patent, thus undermining the concept of utility.¹⁹⁷

In February 1997 the PTO announced that they would allow claims to ESTs based on their utility as probes for the corresponding full-length gene.¹⁹⁸ This was criticized by several institutions, especially by the NIH.¹⁹⁹ To quell the discontent, the PTO assured that a mere allegation of utility as a probe is not sufficient. According to examiners who handle EST patent applications, patent protection is more likely if the following criteria are satisfied: 1) a detailed description of what is being made (i.e. a description of the EST itself); 2) a detailed description of the end use of the invention; 3) examples of how the EST may be used, e.g. by describing what will be probed and 4) if possible, a description of any proteins that correspond to the EST.²⁰⁰

In November 1998, the US PTO granted the first patent for an EST claiming polynucleotides that identify and encode novel human kinases. The patent claims the novel nucleic acid sequences and their use as DNA probes to obtain the full-length human kinase cDNA described in the patent.²⁰¹ Nonetheless, the question of whether an EST patent will block the patenting of the full-length gene is not yet entirely solved. According to John J. Doll, the director of the biotechnology examination at the US PTO, if the claim is limited to the EST itself it does not necessarily preclude

¹⁹³ Oser, 30 IIC1999:1, p. 4.

¹⁹⁴ Maebius, 74 JPTOS 1992:9, p. 654.

¹⁹⁵ Maebius, 74 JPTOS 1992:9, p. 656.

¹⁹⁶ Kight, *Indiana Law Journal*, p. 10 found at www.law.indiana.edu/ilj/v73/no3.kight.html.

¹⁹⁷ Borson, 35 IDEA 1994:4, p. 494-495.

¹⁹⁸ O'Brien, 385 *Nature* 1997, p. 755.

¹⁹⁹ Wadman, 386 *Nature* 1997, p. 312.

²⁰⁰ www.gbpatent.com/ph14.htm

²⁰¹ Robertson, 17 *Nature Biotechnology* 1999, p. 125.

the future patenting of the corresponding full-length gene discovered later. However, this depends on how much information about the gene that is disclosed in the EST patent application. If the gene can be seen as novel and unobvious in light of the EST, as disclosed in the prior art, it may still be patentable.²⁰² In the light of the court decisions relating to the question of nonobviousness, the full-length gene would probably be considered nonobvious, if the test for nonobviousness continues to focus on structural similarity. If the EST does not amount to a significant part of the full-length gene, it seems unlikely that it would be deemed obvious on the ground of structural similarity. However, if the EST covers the full-length gene in a major part, it could be held that they are structurally similar. However, even if this would render the gene *prima facie* obvious, the applicant can rebut this by showing surprising properties of the gene, not possessed by the EST.²⁰³ This argument can be used both ways. An application to an EST when the full-length gene is known in the prior art would undoubtedly be held to be *prima facie* obvious. But if the EST possesses unexpected properties, it may still be patentable.²⁰⁴

The real dilemma is, however, that even if the full-length gene may be patented, the EST patent will be dominant.²⁰⁵ This means that the use of the full-length gene may require a license from the EST patent holder, in order not to infringe that patent. This may, in turn, force the users of the full-length gene to reengineer their gene sequences to include different nucleotides, thus repeating years of experiments in order to avoid patent infringement if a license is not seen as an option.²⁰⁶

4.3.5 The situation in Europe

As has already been observed, the requirements under “utility” and that of “industrial applicability” differ in certain perspectives. The requirement of industrial applicability is regarded as fulfilled if the invention can be used in any kind of industry. “Industry” is interpreted in a broad sense, and it also encompasses research.²⁰⁷ Since ESTs can be used and produced in industry, this could mean that patents on ESTs could more easily be granted under the EPC than in the US. However, for the invention to be patentable, it needs to solve a technical problem. This could mean that it is not enough to state that the EST can be used as a probe to obtain a gene. However, if the gene to be probed is described and the function of that gene is disclosed, the requirement that an invention must solve a technical problem probably would be met.²⁰⁸

²⁰² Doll, 280 Science 1998, p. 690. See also Adler, in Vogel and Grunwald (eds.), p. 32. This argument is also relevant if the ESTs and information about the corresponding gene enters the public domain through publication in any other way.

²⁰³ Eisenberg, 15 Nature Genetics 1997, p. 129.

²⁰⁴ As an answer to the question on whether or not an EST can be considered nonobvious in the light of a patent relating to the full-length gene, the US PTO stated that the entire state of the art as well as the information contained in the application needs to be assessed. Trilateral Project, section 2.3 Inventive step (1).

²⁰⁵ Doll, 280 Science 1998, p. 690.

²⁰⁶ Chahine, 16 Nature Biotechnology 1998, p. 711.

²⁰⁷ Beier and Moufang, in Vogel and Grunwald (eds.), p. 215.

²⁰⁸ Gugerell, in Vogel and Grunwald (eds.), p. 112. See also Straus, 26 IIC 1995:6, p. 934-935.

While the debate about patents on ESTs still raged both in Europe and the US, the EU Directive on the Legal Protection of Biotechnological Inventions slowly took shape. To make clear that ESTs can constitute patentable subject matter, explicit references to “partial sequence of a gene” is incorporated into the Articles of the Directive. For example, Article 5 (2) reads: “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 [...]”. However, Article 5 (3) makes clear that the industrial applicability of such a sequence of a gene must be disclosed in the patent application. To comply with this criterion, the function of the sequence must be disclosed.²⁰⁹ If the EST is to be used to produce a protein or a part of a protein, the applicant must specify which protein or part of a protein that is produced or what function that protein performs.²¹⁰ To reduce the fears that a patent on an EST may block the future patenting on the full-length gene, the recitals clarify that patents for DNA whose sequences only overlap in non-essential parts are not to be regarded as dependent patents.²¹¹ Thus, if the EST does not constitute a major part of the full-length gene, each sequence will be considered as an independent sequence in patent law terms.

In the Trilateral Project, the EPO stated that an EST would normally not be considered as having inventive step in the light of prior art disclosure of the corresponding gene. However, if the EST could be considered as having some unexpected property, it might be patentable.²¹² The patentability requirements for ESTs thus seem to be fairly similar in Europe and in the US. In order to comply with the utility/industrial applicability requirements, the applicant needs to disclose more information than just a statement that it can be used to obtain “a gene”. The gene that is to be probed needs to be specified, and it might even be necessary to disclose the function of that gene in order to obtain a patent on the EST.

4.4 Patenting SNPs

More recently, the patenting debate has centered around SNPs, or single nucleotide polymorphisms. A SNP is a common alteration that occurs in a single nucleotide base in a stretch of DNA. It can be seen as an old and stable mutation.²¹³ Some SNPs are thought to be involved in disease processes, however, the majority probably are not. SNPs can be used as unique and efficient markers when scanning the genome for significant mutations.²¹⁴ In other words, it is a useful tool in finding the exact location of disease genes. The question is whether or not they are patentable. No patents on SNPs have yet been issued. If the novelty, nonobviousness and utility requirements are met they are patentable. To be an invention it must constitute a technically exploitable result. Thus, the determination of such a sequence variation

²⁰⁹ Recital 23 of the Directive.

²¹⁰ Recital 24 of the Directive.

²¹¹ Recital 25 of the Directive. Even if the recitals are not part of the operable part of the directive, they are still significant. Member States do not need to implement the text of the recitals into national legislation but the courts will use the recitals as an aid in interpreting the provisions of that legislation.

²¹² The JPO gave the same answer. Trilateral Project, 2.3 Inventive step (1).

²¹³ Marshall, 227 Science 1997, p. 1752.

²¹⁴ Marshall, 227 Science 1997, p. 1752.

would remain a discovery until it is affiliated with a result that can be used in technology. Such a use could be an established link between the SNP and a clinical illness.²¹⁵ Another use could be to trace parentage or ancestry.²¹⁶ The same debate surrounding the patenting of ESTs also encompass SNPs, i.e. the fear that such patents would impede cooperation among laboratories and limit the ready accessibility to data and materials to researchers.

4.5 A new kind of protection?

Some argue that biotechnological inventions do not fit into the mechanically based norms of patent law and that some other form of protection is needed.²¹⁷ The patent system has also been criticized for producing certain detrimental effects. Obtaining patent protection is costly and time-consuming. To maintain protection the inventor needs to pay an annual fee as well as take measurements against infringers. In addition, patents discourage short-term dissemination of information. One alternative form of protection that has been suggested is copyright. The idea is that the sequence of letters representing the amino acids or the nucleotides is an original literary work. One major problem with this, however, is that copyright does not protect against independent retrieval. If someone else would retrieve a DNA sequence containing the same information as an earlier sequence, this would not constitute infringement. Thus, in infringement considerations this system would probably prove to give inadequate protection for biotechnological inventions. Another alternative would be trade secrets. However, trade secrets do not offer protection if the product can easily be analyzed by competitors once it has been put on the market. From society's point of view, trade secrets are not effective since they do not disclose the invention, leading others to repeat research, finding solutions to problems already solved. A third suggestion is the creation of a *sui generis* right. This was done to protect new plant varieties, by adopting the International Union for the Protection of New Varieties of Plants (UPOV). The argument against a *sui generis* right is that this would lead to fragmentation and over-regulation of intellectual property rights, leading to more confusion. It would also confer practical and time-consuming difficulties in introducing such a system, especially on an international level.²¹⁸

Another alternative is to offer patent protection with a narrower scope of protection than patents granted today for biotechnological inventions. The main concern now is that once a product is patented, that patent extends to any use, even those that have not been disclosed. The suggestion is thus to give the patent applicant protection only for the use specified in the application, leaving further patenting of the invention free to those who come up with a different application of the invention.²¹⁹ The situation thus resembles patent on second medical indication. However, the biotechnology industry strongly opposes such suggestions, arguing that there is no good reason why their inventions should receive less protection than inventions in the field of chemistry or other related technologies.

²¹⁵ Oser, 30 IIC 1999:1, p. 7 n. 22.

²¹⁶ Doll, 280 Science 1998, p. 690.

²¹⁷ Ko, 102 Yale Law Journal 1992, p. 777.

²¹⁸ Beier and Moufang, in Vogel and Grunwald (eds.), p. 210.

²¹⁹ See Koktvedgaard, NIR 1994:4, p. 442.

This leads us back to the patent system. Those who argue in favor for this kind of protection point to the fact that the patent system has historically been able to cope with every new kind of technology that has emerged. Even if the patent system was not initially conceived to protect biological inventions, it must be possible to offer protection to new kinds of inventions emerging from the development of technology. Indeed, the patent system has proved flexible enough to also encompass the protection of human genes without too many difficulties. It can thus be argued that it would be unnecessary to make detailed changes in the intellectual property system only to fit a particular technology.

People opposing the patenting of DNA *par se* often suggest a patent to the process of obtaining the gene as an alternative. They feel that the argument that genes can be invented is strained and contend that a gene only can be seen as a discovery. However, the process to identify and isolate that gene is a result of human ingenuity and therefore patentable. When the patent claim is to a DNA sequence *per se*, its effect is to exclude others from using that sequence for any purpose, even though only one use for it was recognized by the inventor.²²⁰ Process patents can be seen to somewhat limit the extent of that monopoly. However, it is generally believed by the biotech industry that it is easy for others to “engineer around” such patents to produce the same product in a new way, process patents thus being too easy to circumvent.²²¹ Generally, process patents are narrower in scope and more difficult to enforce than product patents. Such patents are therefore considered not to offer adequate protection to biotechnological inventions.

4.6 Conclusions

As we have seen in this chapter, it is possible for genes *per se* to be the object of patent protection. What is it then that makes a gene a patentable invention? For patent purposes, the DNA molecule is characterized as a chemical compound. Decisions in this area had already clarified that naturally occurring chemicals, such as e.g. adrenaline, could be patented. The determining factor is, however, that a naturally occurring compound must be extracted from its natural state. The genes as present in our bodies are mere discoveries and as such not patentable. It is not until the gene is located, cloned and sequenced that it can be considered as a patentable invention.

Even though the gene is pre-existent in nature and hence not created by man, it is considered novel when it is put at society’s disposal for the first time. The isolation and cloning of the gene outside the human body are results of technical manipulation. Since this cannot be accomplished by nature alone, the gene can be considered as a product of human ingenuity. This standpoint is further emphasized in the case of cDNA sequences. A cDNA sequence is not a true copy of the genomic DNA, as it only contains the protein-encoding regions of the gene. According to the Opposition Division of the EPO in the Relaxin-case, since cDNA sequences as such do not exist in nature, these sequences can be considered novel for this reason alone.

²²⁰ Doll, 280 Science 1998, p. 690.

²²¹ Barton, 26 IIC 1995:5, p. 609.

However, the most difficult hurdle for patenting full-length DNA sequences is the nonobviousness requirement. Does an amino acid sequence placed in the public domain suggest the corresponding DNA sequence since the genetic code can be used to link the two? Or does the redundancy of the genetic code mean that the DNA sequence cannot be contemplated, and therefore not be considered obvious? The answer to these questions seems to be dependent upon the length and structure of amino acid sequence. The harder it would be to envision the structure of the DNA sequence in question, the likelier it is that the gene will be considered as nonobvious. Recent developments in the US might suggest that the nonobviousness assessment also depend upon the specificity with which the prior art teaches the technique how to obtain a specific gene. The more detail in the prior art on how to obtain a particular gene, the greater the possibility that the gene will be rendered obvious. This development might somewhat curb the criticism that the patentability of a DNA sequence seems to depend not on the level of inventive skill necessary to obtain it but on the absence of structurally similar sequences disclosed in the prior art. It is generally believed that patents should only be granted for inventions that contribute to the advancement of science. Many argue that it is not a scientific achievement to obtain the gene knowing the corresponding amino acid sequence, since this would eventually be the result, given time and financial resources. Allowing patents on inventions that can be obtained through some routine experimentation might undermine the nonobviousness requirement. This is recognized in Europe and Japan, where a DNA sequence lacks inventive step if there is a high probability to obtain it, given the protein or amino acid sequence.

On the flip side of the predictability criterion is the disclosure requirement. Here, a person skilled in the art should be able to obtain the gene without undue experimentation if presented with the description of the invention. Hence the expectation of success is a determining factor, limiting the scope of allowable claims. Disclosure is the justification of the exclusive market position conferred to the patent holder and it must therefore be precise enough to enable someone to reproduce the totality of the invention as claimed. Biotechnology is still at a relatively early stage of development and, as in many new markets, this is characterized by broad patents being granted. However, as the technology is beginning to mature, the protection offered is getting narrower in scope. When it comes to generic claims, encompassing a large number of DNA molecules, the requirements seem to differ somewhat between the US and Europe. The US has tended to hold biotechnology inventors to a relatively high disclosure standard, clarifying that defining scope in terms of biological activity of the gene is not enough. Where the EPO traditionally has been less stringent, recent case law in the EPO seems to indicate a change of direction, requiring a higher level of disclosure.

As with all patentable inventions, DNA sequences must have a demonstrated practical use. Thus, it is not enough merely to determine the nucleotide sequence of the gene. In order for the gene to be a patentable invention, its function must be established. The protein encoded by the gene must be verified and its biological activity described. While it is indeed harder to establish the biological function of a gene than it is to characterize it by its nucleotide sequence, the utility requirement is generally a low hurdle to overcome for full-length DNA sequences. However, it can pose a problem for those who wish to seek patent protection for uncharacterized

partial sequences of a gene. A common mistake amongst such applicants has been to provide only a general description of potential applications of ESTs. In order for a patent application to an EST to succeed, it seems that more specific information about the utility for each individual EST sequence needs to be disclosed. A patent application claiming the EST as a probe to determine the chromosome location of the full-length gene probably needs to specify the gene to be probed and possibly even the function of that gene. Patents on ESTs have been discussed also in relation to its impact on full-length gene patenting. However, given the focus on structural similarity, it seems unlikely that a disclosure of a small fragment would render the whole gene obvious.

5. ETHICAL PERSPECTIVES

Now having established that it is indeed possible to patent human DNA sequences, there are still some last considerations to be made before a final conclusion can be made. An assessment need to be made whether patent applications relating to inventions of DNA sequences should be denied for moral and ethical reasons. Gene patenting is a highly controversial subject. However, this can be dealt with by special regulations safeguarding certain fundamental ethical values. Attempts have been made to introduce specific exclusionary provisions into the patent systems in order to draw a more precise borderline between the ethically permissible and the unacceptable when it comes to inventions. Ethically founded reservations are important in the area of inventions with regard to the human body. The far-reaching possibilities of modern biotechnology and genetic engineering have increased the risk of achieving inventions that are ethically unacceptable and therefore not worthy of being protected by the legal system. Consequently ethical considerations have been transformed into legal rules, excluding certain inventions from the category of patentable subject matter. Thus, under the European Patent Convention and the Japanese Patent Act, an ethical examination is part of the requirements for patentability.²²²

5.1 What a patent is not

It is important to understand that a patent is not a rule for ethics and not an authorization for sale. A patent is a purely competitive device to prevent an invention's commercial use by third parties, it does not authorize the holder to implement his invention.²²³ Nor do they confer rights of possession over anything.²²⁴ Thus, patent protection is merely an exclusionary position, it does not mean that the patentee can actually use his invention, let alone exploit it industrially. The granting of a patent does not constitute an official sanction of the value or desirability of the

²²² According to the Japanese Patent Act Sec. 32, inventions liable to contravene public order, morality of public health shall not be patented.

²²³ See, for example, Recital 14 of the Biotechnology directive.

²²⁴ Schatz, 28 IIC 1998:1, p. 13.

invention.²²⁵ The patent holder is only entitled to use his invention within the framework of the overall legal system. Other laws, such as regulations concerning genetic engineering, safeguard what is actually legal to perform. The refusal of a patent application does not mean that the invention cannot be used or exploited. On the contrary, it can be used by anyone – subject again to the law in general.²²⁶ Thus, an inventor, regardless of whether or not he is granted a patent, must attend to all legal regulations that might prevent the working and the exploitation of the invention.²²⁷ Therefore it can be argued that patent law is not a suitable instrument for preventing abuses or fending off risks which a given technology might cause.

5.2 Does ethics belong in the patent system?

There is a debate on whether or not the patent authorities should make ethic considerations before issuing a patent. Some people think that a patent office is not the place for creating policy on scientific research. Since the role of the patent system is to stimulate and reward innovation, it should not deal with moral and ethical issues or determine scientific policy. They argue that morality and ethics are not properly debated in the area of patent law. Instead, these are issues that the legislator should address while discussing appropriate regulations for biotechnology research as a whole.²²⁸ Many people opposing the patenting biotechnological inventions on moral grounds are more opposed to the existence of the science itself than the existence of patents on the inventions.²²⁹ However, it can be argued that denial of patent protection is not an appropriate or effective means of conduct control. Harm from the misuse of technology should not, according to this view, be grounds for denial of patent protection, but should be addressed in separate legislation regulating the research itself. When the invention has reached the stage of patent application, a lot of research has already been done. Other laws, that can be applied in an early stage would be more appropriate. In the words of the US Supreme Court in the case of *Diamond v. Chakrabarty*: “The grant or denial of patents [...] 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 Canute could command the tides.”²³⁰

Nonetheless, many people opposed to the science itself are also opposed to the patenting of biotechnological inventions since the theory behind the patent system is to promote research and innovation. If research in the biotechnology area is deemed as unwanted, patents will also be regarded with disapproval, since they encourage innovations in this field. Some critics focus on the fact that genes are a phenomenon of nature which cannot be invented by man. Man did not create the genes and the inventor is only to a small degree responsible for the existence of his invention.

²²⁵ Crespi, EIPR 1995:9, p. 435.

²²⁶ Schatz, 28 IIC 1998:1, p. 12.

²²⁷ Moufang, 25 IIC 1994:4, p. 503.

²²⁸ Walter, Indiana Law Review, p. 6, found at www.law.indiana.edu/ilj/v73/no3/walter.html.

²²⁹ Walter, Indiana Law Review, p. 8

²³⁰ *Diamond v. Chakrabarty*, 447 US at 317.

However, to refute this it can be argued that every inventor has to use natural forces and preexisting components and inventions relating to genes does not differ from other inventions in this respect.²³¹ Yet another group of people disputing the patenting of biotechnological inventions is opposed to the idea of “monopolizing” genes. They argue that genes are “the common heritage of mankind” and that genes should be freely accessible to researchers.²³² Quite a few scientists can be found in this category.

The rationale behind moral clauses in patent law is to prevent the impression being given that an invention, whose use would be contrary to legal fundamentals or offend the sense of decency, bears the seal of society’s approval.²³³ Patent laws are seen as being part of the value system of society and they should therefore not contradict this system.²³⁴ The question is then how detailed these “ethical clauses” should be. Many argue that it is only for the legislator to create the policy concerning which inventions that should be patentable and that the patent laws therefore should be detailed, allowing little or no discretion to the patent office. Others argue that since the legislator cannot deal with all questions in advance, it should only provide the normative framework. The patent office should therefore be given some discretionary power to determine such questions on a case to case basis.²³⁵

According to the TRIPs Agreement, it is allowed to deny patenting of inventions on the grounds of ethical concerns. According to Article 27.2:

Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect public order or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by domestic law.

This article was a result of a compromise between differing opinions in the negotiation of the agreement. There were widespread disagreements on the issue of patentable subject matter between different countries. The US, Japan and certain European countries wanted no or minimal exceptions to patentable subject matter, whereas other countries in Europe and the developing countries wanted to exclude certain inventions from patentability altogether.²³⁶

5.3 Article 53 (a) EPC

Article 53 (a) EPC can be seen as a specific “gate of entry” for ethical considerations. The article provides that patents shall not be granted for “inventions the publication or exploitation of which would be contrary to ordre public or

²³¹ Beier and Moufang, in Vogel and Grunwald (eds.), p. 209.

²³² Vogel, in Vogel and Grunwald (eds.), p. 10.

²³³ Schatz, 28 IIC 1998:1, p. 12.

²³⁴ Vogel, in Vogel and Grunwald (eds.), p. 10.

²³⁵ Berman, discussion in Vogel and Strauss (eds.), p. 40. See also Grunwald, in Vogel and Grunwald (eds.), p. 102.

²³⁶ Ford, EIPR 1997:6, p. 315.

morality”. According to the Guidelines of the EPC, the purpose of this regulation is to “exclude from protection inventions likely to induce riot or public disorder, or lead to criminal or other offensive behaviour”. The provision is thus only likely to be involved in rare and extreme cases.²³⁷

The first thing to notice is that the act that is to be measured against ordre public and morality is not the patenting itself of the invention but if the publication or exploitation of the invention would be contrary to any of the two standards. The decisive questions are what ordre public and morality mean. Ordre public can be understood as aiming at protecting public security and the physical integrity of individuals.²³⁸ However, Article 53 (a) should not be viewed as a general clause for value judgements of the EPO.²³⁹ Instead, ordre public should be determined with reference to the actual legal order applying in the Contracting States. Article 53 (a) EPC is only violated where the conflicting norm constitutes one of the fundamental principles of the legal systems. Such values can be expressed in e.g. criminal law or constitutional law protecting basic rights.²⁴⁰ Nowhere in the Contracting States is genetic engineering forbidden. Under these circumstances the EPO cannot consider inventions relating to genetic engineering as being generally against ordre public.²⁴¹ However, the prevailing opinion is that inventions should not be patented if they degrade human beings to objects of technology.²⁴² The EU Biotechnology Directive may also have influence on these considerations, since the rules laid down in the Directive are to be implemented into the laws of the EU Member States. Another instrument that can be considered to implement essential values in Europe is the European Convention on Human Rights (ECHR). ECHR has been ratified by all EPC member states and therefore the obligations stemming from it are binding on those states. It can therefore be argued that the ECHR should be the legal basis of an ethical examination of patent applications.²⁴³ The convention lays down, for example, a prohibition of treatment that violates a human dignity (Art. 3).

The concept of “morality” is another thing that the patent office cannot define for itself, but a question of actual codes of behavior, which are founded on generally accepted norms rooted in the European culture.²⁴⁴ Thus, the use of an invention would be contrary to morality only if it would be objectionable by society in general, or at least by the professional and commercial circles concerned.²⁴⁵ One example would be an invention which genetically modified the human body in order to be able to use it as a “factory” of valuable substances of organs.²⁴⁶

If the invention can be used *only* in a manner which would violate ordre public or morality, it should not be patented. However, the assessment should be based on the inventions claimed use, not some merely possible use. The assessment should thus not concentrate on possible misuse. The mere risk of a new technology is not enough

²³⁷ Guidelines for examination in the European Patent Office, C-IV 3.1.

²³⁸ Holtz, NIR 1996:1, p. 24.

²³⁹ Straus, 26 IIC 1995:6, p. 949.

²⁴⁰ Schatz, 28 IIC 1998:1, p. 14.

²⁴¹ Straus, 26 IIC 1995:6, p. 948. See also Teschemacher, NIR 1994:1, p. 53-54.

²⁴² Moufang, 25 IIC 1994:4, p. 505.

²⁴³ Ford, EIPR 1997:6, p. 315.

²⁴⁴ Holtz, NIR 1996:1, p. 24

²⁴⁵ Schatz, 28 IIC 1998:1, p. 14.

²⁴⁶ Beier and Moufang, in Vogel and Grunwald (eds.), p. 214.

to outweigh the right of the inventor to receive a patent.²⁴⁷ However, the interests have to be carefully balanced. According to the Guidelines of the EPO, the refusal of a patent may not be necessary in some cases. If the invention has both an offensive and a nonoffensive use, the invention can still be patented as long as the application does not contain an explicit reference to a use which is contrary to ordre public.²⁴⁸

In the case of Howard Floney Institute/Relaxin²⁴⁹, the EPO had granted a patent in which one of the claims comprised a DNA fragment encoding human H2-preprorelaxin. Relaxin is a human hormone naturally produced in a woman's ovaries at the onset of labor, and its function is to relax the muscles used in giving birth. The hormone is produced by a gene which is only activated at this particular time. The relaxin DNA had therefore been isolated from a tissue taken from a pregnant woman. The patent was opposed by the Green Party of the European Parliament, who stated that such an invention should not be patentable under Article 53 (a) EPC. They argued essentially as follows: 1) in order to put the invention into practice, tissue had to be taken from a pregnant woman, which is immoral and constitutes an offense against human dignity; 2) the patenting of human genes "amounts to a form of modern slavery since it involves the dismemberment of women and their piecemeal sale to commercial enterprises". This infringes the human right to self-determination. Finally, they argued that 3) the patenting of human genes means that human life is being patented. This was considered to be intrinsically immoral.²⁵⁰

On the first ground, the Opposition Division concluded that, as long as the subject from whom human tissue was taken consented to the taking of that tissue, there was nothing immoral in the mere act of taking tissue, since this is a standard practice in medical procedures.²⁵¹ As for the opponents' assertions concerning slavery and the dismemberment of women, the Opposition Division concluded that this betrayed a fundamental misunderstanding of the effects of a patent. Since patents on human genes do not confer on their proprietors any right whatsoever to individual human beings, no question of slavery arose. The exploitation of the invention did 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; there is therefore no need to use human beings as a source for the protein.²⁵² On the final argument that the patenting of human genes was immoral since it was tantamount to patenting life, the Opposition Division's position was that DNA is not life, but a chemical substance. The patenting of a single human gene has nothing to do with the patenting on human life.²⁵³ Finally, the Opposition Division noted that exceptions to the grant of patents for inventions under Article 53 (a) should only occur "in those very limited cases in which there appears to be an overwhelming consensus that the exploitation or publication would be immoral".²⁵⁴

²⁴⁷ Grunwald, in Vogel and Grunwald (eds.), p. 102.

²⁴⁸ Guidelines for examination in the European Patent Office, C-IV 3.3.

²⁴⁹ Relaxin EP-B1 112, 149, OJ EPO 1995, 388. 27 IIC 1996:5, p. 704.

²⁵⁰ Relaxin EP-B1 112, 149, OJ EPO 1995, 388. 27 IIC 1996:5, p. 704. Section 6.1 of the decision.

²⁵¹ Relaxin, Section 6.3.1 of the decision.

²⁵² Relaxin, Section 6.3.3 of the decision.

²⁵³ Relaxin, Section 6.3.4 of the decision.

²⁵⁴ Relaxin, Section 5.5 of the decision.

This decision of the Opposition Division thus shows that the application of Article 53 (a) is not likely in questions concerning the patenting of human genes per se. Such a patent can generally not be seen as contrary to ordre public or morality.

5.5 The situation in the US

There are no rules in US patent law giving the US PTO the authority to stop the issuing of a patent on moral grounds alone. However, when Jeremy Rifkin, a biotechnology opponent, and Stewart Newman, a biologist at New York Medical College, applied for a patent in December 1997 on methods for creating a human-animal chimera, the US PTO claimed they had such authority.²⁵⁵ The applicants held that their intention was to raise a broad public and legal debate about the implications of such a patent with the aim of blocking further research in the area.²⁵⁶ Transgenic animals, such as mice with a human oncogene, used in cancer research, and pigs carrying human genes to make their organs suitable for transplantation to humans, are already patented. The applicants feared that drug testing and disease studies will one day feature animals that are too human-like.²⁵⁷ In April 1998, the US PTO issued a statement asserting that the PTO's legal authority allows it to deny patents based on moral grounds. The statement claimed it was in the position of the PTO that inventions directed to human/non-human chimeras could not be patentable because they would fail to meet the public policy and morality aspects of patent law.²⁵⁸ This "morality requirement" is rarely used and is based on *Lowell v. Lewis*²⁵⁹, a Massachusetts circuit court decision from 1817. In that case, the Court found that the utility requirement included a moral component. It stated: "All that the law requires is, that the invention should not be frivolous or injurious to the well-being, good policy, or sound morals of society. [...] For instance, a new invention to poison people, or to promote debauchery, or to facilitate private assassination, is not a patentable invention."

However, the biotechnology industry was not happy about the PTO's alleged authority to rule on morality issues. They claim that the patent office should not create policy on scientific research and hold that such issues should be dealt with by the legislator. There is now uncertainty in the industry on how many human genes a transgenic animal can possess before it is considered to be immoral.

5.6 The John Moore case

A somewhat different issue than the patenting of genes is the question concerning the ownership of parts of the human body. Does a human being "own" the parts of his or her body? If human tissue is used for commercial purposes without the knowledge or

²⁵⁵ Wadman, 393 Nature 1998, p. 200.

²⁵⁶ Deger, A Chimeral Patent, p. 1, found at www.ipmag.com/98-jun/deger.html.

²⁵⁷ Deger, A Chimeral Patent, p. 2.

²⁵⁸ Wadman, 393 Nature 1998, p. 200.

²⁵⁹ *Lowell V. Lewis*, 15 F.Cas. 1018 (no. 8568) (1817).

permission of the person from whom the material was obtained, is this theft of that person's property? These questions were addressed in the California Supreme Court case *John Moore v. The Regents of the University of California*.²⁶⁰ Moore was a patient at a University of California hospital, suffering from hairy-cell leukemia. In 1976 Moore's spleen was removed as part of the treatment by his physician, Dr Golde. Prior to the operation Golde and Quan, a researcher employed by the UC, made arrangements to obtain portions of the spleen following its removal and take them to a separate research unit. However, neither Golde nor Quan informed Moore of their plans to conduct this research or requested his permission. Using the tissue removed from Moore, Golde established a cell-line from Moore's T-lymphocytes. A T-lymphocyte is a type of white blood cell, producing proteins that regulate the immune system.²⁶¹ In 1991 the Regents applied for a patent on the cell-line, listing Golde and Quan as inventors. When the patent was issued in 1994, Golde entered into contracts with Genetics Institute, a biotechnology company, and Sandoz, a pharmaceutical company, to explore the commercial potential of the cell-line and derivative products. When Moore found out what was going on, he sued the UC for failing to obtain his consent, for breach of fiduciary duty and for conversion²⁶² of his body tissue. Ruling on the issue of whether Golde had failed to disclose preexisting research and economic interests before obtaining consent to the medical procedures, the Court held that a physician must disclose personal interests, whether research or economic, unrelated to the patient's health that may affect the physician's professional judgement.²⁶³ Concluding that Moore had not received information of Golde's intent to obtain a portion of Moore's spleen the Court accepted Moore's allegation of breach of fiduciary duty and lack of informed consent.

However, the Court came to another conclusion on Moore's proprietary claim to the cells and the cell-line developed from his spleen. The proprietary action was rejected on both practical and policy grounds. Because California statutory law drastically limits a patient's control over excised cells, there was nothing left to be treated as property.²⁶⁴ In any case, the patented cell-line was held to be both factually and legally distinct from the cells taken from Moore's body. For cells to become a cell line, they must be adapted to laboratory conditions. In the process, the cells change and often become abnormal.²⁶⁵ The Court thus held that the cell-line was a new invention and different from Moore's cells, which meant that Moore's allegation that he owned the cell-line was inconsistent with the patent.²⁶⁶ The Court then went on to consider relevant policy questions. The Court felt that an extension of conversion law into medical research would hinder biotechnological research and hamper development in this area. The rationale behind this was that biological material is often distributed to other researchers who may be unaware of inadequate disclosures violating the patient's rights. If these researchers could be held liable for conversion, this could have the effect as to hinder research by restricting access to necessary raw materials.²⁶⁷ In the words of the Court "the theory of liability that Moore urges us to

²⁶⁰ *Moore v. The Regents of the University of California*, 793 P.2d 479 (Cal. 1990).

²⁶¹ *Moore*, 793 P.2d at 481 n. 2.

²⁶² Conversion is the unlawful turning or applying the personal goods of another to the use of the taker, or of some other person than the owner.

²⁶³ *Moore*, 793 P.2d at 483.

²⁶⁴ *Moore*, 793 P.2d at 491.

²⁶⁵ *Moore*, 793 P.2d at 492, n. 35.

²⁶⁶ *Moore*, 793 P.2d at 493.

²⁶⁷ *Moore*, 793 P.2d at 494.

endorse threatens to destroy the economic incentive to conduct important medical research. If the use of cells in research is a conversion, then with every cell sample a researcher purchases a ticket in a litigation lottery.”²⁶⁸ The Court concluded that it was not for them to make a decision on whether the scientific users of human cells are to be held liable for failing to investigate consensual pedigree of their raw materials. Instead this should be a question of the legislature, which has a greater ability to gather empirical evidence and solicit the advice of experts.

The Court hence made clear that an invention developed from a tissue is different from the tissue itself, and that the donor therefore cannot have any right in the patented invention. Moreover, if the donor were to be granted property rights in anything developed from the tissue, this would inhibit research, to the detriment of society in general. The societal interest in protecting the biotechnology industry from possible lawsuits relating to proprietary issues was thus considered being of greater importance than the individuals interest in his excised tissue.

5.7 The EU Directive

To ward off ethical objections, certain articles were incorporated into the directive to clarify the scope of patentable subject matter. The directive can be seen as aiming at establishing an EU-wide framework of rules on the ethics of particular biotechnological inventions.²⁶⁹ Article 6 is similar to the “ethical clause” in EPC, also excluding from patentability inventions whose exploitation would be contrary to *ordre public* or morality. Subsection (2) of the article contains a non-exclusive list of inventions that should be deemed to be unpatentable. The following are examples of inventions that should be excluded from patentability: processes for cloning human beings; processes for modifying germ line genetic identity of human beings²⁷⁰ and uses of human embryos for industrial or commercial purposes. These examples are supposed to be a general guide for interpretation of the *ordre public* and morality criteria for the national courts and patent offices.²⁷¹ However, it is important to remember that this list is not exhaustive and that other processes that offend against human dignity also should be excluded from patentability. It is deemed that patent law always should be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person.²⁷² In the light of the development in the US, the recitals make clear that a process to produce chimeras of human and animal cells should not be patented.²⁷³ Moreover, being influenced by the case of Moore in the US and the Relaxin case under the EPO, the recitals state that “if an invention is based on biological material from human origin or if it uses such material, where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent

²⁶⁸ Moore, 793 P.2d at 495-496.

²⁶⁹ Rothley, 26 IIC 1995:5, p. 669.

²⁷⁰ Germ line therapy alters the genetic identity not only of one individual, but also of its descendants.

²⁷¹ Recital 38 of the directive.

²⁷² Recital 16 of the directive.

²⁷³ Recital 38 of the directive.

thereto, in accordance with national law.”²⁷⁴ However, this requirement of free and informed consent is not coupled with any kind of sanction. Recital 27, which concerns patents relating to biological material derived from plants and animals, notes that the patent application should include information on the geographical origin of such material. However, recital 27 goes on to say that this reporting obligation is without prejudice to the processing of the patent application or the validity of rights arising from the granted patent. In contrast, recital 26 contains no such exemption. Thus, the situation is unclear on how national legislation or national courts will deal with a situation similar to the one in Moore; i.e. whether or not the patent would issue even if proper consent had not been given from the originator of the tissue. Finally, the recitals also remind that the European Union is to respect fundamental rights, as guaranteed by the ECHR.²⁷⁵

5.8 DNA as a chemical compound

Another issue connected to ethical considerations is the question of whether DNA should be compared to chemical compounds. The DNA molecule is indeed a chemical compound and it is also treated like one when it comes to patent law. However, many still feel that it is disturbing to compare DNA, which determines the conditions for our existence, like health, intelligence and appearance, with an ordinary “lifeless” chemical compound. The argument is that the human genome, as different from most other chemical compositions, is finite. When the 100 000 or so genes in our body are all patented, no more can be invented. Many see our genes as “the common heritage of mankind” that should be free for all, and not subject to any kind of proprietary restraints. Another argument that I have already touched upon, is that the important quality of the genes lies not in the fact that it is a chemical but in the fact that it is an information carrier.²⁷⁶ The role of the DNA in the body is vastly more important than any other chemical compounds present in our bodies. A third point is that we have feelings in connection with our genes that we don’t have towards other inventions.²⁷⁷ The genes in our body are intimately associated with our bodies and personalities and a claim to a DNA as a chemical compound may therefore be seen by some as disturbing. However, the characterization of DNA as chemical substances has generally meant good news to the biotechnology industry, who has therefore had little motivation to challenge the analogy.²⁷⁸

5.9 Conclusions

A patent should not be seen as an assessment on the desirability of the invention in question. However, in order not to undermine the credibility of the patent system, there are certain ethical safeguards incorporated in the patent laws. These clauses are designed to prevent ethically unacceptable inventions from giving the impression

²⁷⁴ Recital 26 of the directive.

²⁷⁵ Recital 43 of the directive.

²⁷⁶ Koktvedgaard, NIR 1994:4, p. 441.

²⁷⁷ Koktvedgaard, NIR 1994:4, p. 441.

²⁷⁸ Eisenberg, 15 Nature Genetics 1997, p. 125.

that they are accepted by society. Nonetheless, only those inventions which are contrary to the legal fundamentals of society should be excluded from patentability. Thus, such exceptions are based on values actually expressed in the legal system and it is not a *carte blanche* for discretionary value judgements of the patent authorities. Decisions are taken on a case by case basis and no general exceptions relating to specific fields of technology exist. Only a possibility of misuse is not enough for these ethical clauses to kick in. The assessment is made only on the use of the invention as described in the patent application. However, it must be understood that a granted patent does not mean that the patent holder can do whatever he pleases. Naturally, all laws of society must be obeyed when exploiting the invention, notwithstanding the patent.

The situation in the US is somewhat different. No statutory exclusion from patent protection exists for ethically questionable inventions. Even if ethical arguments have been raised in the US, the only principle that the US PTO can lean against in order to challenge patents on moral grounds is a very seldom used court decision which dates as far back as 1817. In addition, this decision originates from an inferior state court, and its status might thus be questioned. This might suggest that the moral issue in patent law has a somewhat subordinate position in the US compared to Europe and Japan.

6. ECONOMIC PERSPECTIVES

6.1 The significance of patents for technical development

Even if the patent system has its critics, it still plays a significant role for technical progress. Patent protection is a way for society to promote innovation, by offering a prospect for reward for it. The temporary commercial exclusivity granted by a patent is necessary to encourage investors to fund expensive, long term and high-risk areas of research. Further research is encouraged by publication, which provides researchers with a springboard from which to make further improvements and new inventions. The development of science made by inventions is in turn of great importance of the economic development. Without an ample protection, growth in industry risks stagnation, harming economic growth.

6.2 Tragedy of the anticommons?

However, there is a theory that patents can actually deter, and not encourage, the development of new inventions. In contrast to the “tragedy of the commons”, which means that a resource is prone to overuse when too many can use a resource and no-one has a right to exclude another, the “tragedy of the anticommons” arise when too many owners can block each other.²⁷⁹ This might lead to underuse of scarce

²⁷⁹ Heller and Eisenberg, 280 Science 1998, p. 698.

resources. If too many patents are granted on upstream technology, this will obstruct further downstream research and the development of useful products. The theory of anticommons is especially developed in relation to EST patents. If a patent is granted to an EST, anyone who wants to use the full-length gene containing the EST sequence will have to obtain a license from the EST patent holder. Since there can be several ESTs relating to the same gene, multiple licenses might be needed.²⁸⁰ The argument is that if multiple licenses are needed, the difficulties and transaction costs also multiply. This might discourage researchers to obtain the full-length gene. However, this debate extends to other research tools as well, not only ESTs. Any large research project might call for access to many different research tools, and the cost and administrative burden might thus mount quickly. This is a problem since it is the discovery of the full-length gene and its functions that are of value to society.²⁸¹ Hence, there is a need to strike a balance between public access to research tools and private property.

Another concern is reach-through license agreements on sales of products that are developed partly through the use of licensed research tools. Such an agreement gives the patent holder on an upstream research tool rights in subsequent downstream inventions. One example of such a right might take the form of a royalty on sales. Such reach-through clauses offer some advantages both to the researcher and the patent holder. Researchers with limited funds are able to use the research tool freely until the research gives valuable result. The patent holder can then reap the benefits of such future inventions. However, in practice such agreements might lead to an anticommon. Each reach-through royalty obligation becomes a prospective “tax” on the sale of the new product. The more research tools that are used in developing a product, the higher the “tax” burden. The conclusion is then that intellectual property rights offers both promises and risks. A policy that lead to too many upstream rights might actually lead to fewer useful products for improving human health. However, questions relating to licensing are not really an issue of patent law, but a transfer of technology policy.

6.3 Broad patent claims

A further concern is that patents issued on biotechnological inventions have a tendency towards being unduly broad in scope. The reason for such broad scope is that once a gene has been cloned and sequenced, it is relatively simple for someone else to obtain analogs to that gene. For the patent not to be circumvented in this way, a broad patent scope is sought, claiming all possible variants to the gene. A patent that could easily be circumvented would be commercially valueless, and investors would not support the cost for obtaining the gene in the first place since the returns for investment would be low if exclusivity cannot be assured. There is also an argument that the scope of the patent should correspond to the importance of the invention.²⁸² Therefore, “pioneer inventions” are usually given broader protection

²⁸⁰ Robertson, 17 *Nature Biotechnology* 1999, p. 125.

²⁸¹ Even if there are research exemptions in most patent systems, the scope of such an exemption is unclear and therefore even scientists involved in basic research might prefer to obtain a license, lest they risk being sued for patent infringement.

²⁸² Barton, 26 *IIC* 1995:5, p. 611.

than less significant inventions, since the idea is that inventions that start a new industry should be especially rewarded. The problem is that too many biotech patent applications are very broad in scope. Overly broad patent scopes can reduce the social benefit of patents, since they tend to discourage further research in the area.²⁸³ Broad patent claims thus increase the incentives to initial investors and inventors at the expense of decreased incentives to later ones.²⁸⁴ Another argument against broad patent claims is that the scope should not be broader than the description of the invention. Since the justification of the patent monopoly lies in the disclosure of the invention, the scope should not be broader than the ability of a person skilled in the art to reproduce the entire invention as claimed. Thus, while broad scopes can be justified in certain circumstances, they might also pose barriers to future inventions. However, in recent years, patent offices and courts have tended to be more restrictive when it comes to allow broad patent claims, as can be seen both in the US and in Europe.

6.4 National and International Interests

The searching for human genes has obvious benefits for humanity. To reach an understanding of the functions of the genes and their potential use in the development of pharmaceuticals is an important issue for all nations. The Human Genome Project should therefore be a project of international collaboration. The research workers and the public bodies in each country want to play a part in this international collaboration, with the potential of advancing the understanding of human biology and medical knowledge. However, they also have an obligation to safeguard any possible return to the national economy if any commercially valuable inventions are made during this research. One of the reasons the NIH filed for patent protection of the EST sequences manufactured in the course of research within the HGP is believed to be an attempt for the US, having borne the major part of the bill for the HGP, to recover some of its investments.²⁸⁵ These patent applications were believed to be in the best interest of the public, but the fear expressed by many was that this would induce a “genome gold rush” where each country want to ensure their domestic economic development rather than looking to increase general scientific knowledge on the biological functions of the human body.

The effectiveness of protection of inventions is critical to any industry. To be able to attract investments, the countries must offer to their industries a healthy environment. The biotechnology industry is thus dependent upon patent protection to maintain its ability to compete in a highly competitive world market. The biotechnology industry therefore puts pressure on policy makers to give it ample protection, otherwise threatening to move where better protection is given. Since growth in industry will translate into products, jobs and wealth, the national governments seek to employ rules that would be advantageous to industry. It is for this reason that the EU directive came about. The European Biotechnology industry lagged behind developments in the US and Japan, and the reason for this was believed to lie in part

²⁸³ Ko, 102 Yale Law Journal 1992, p. 792-793.

²⁸⁴ Barton, 26 IIC 1995:5, p. 611-612.

²⁸⁵ Byrne, 15 World Patent Information 1993:4, p. 200.

in the fact that investors were insecure about the protection conferred to biotechnological inventions. The US also changed its scope of protection a few years ago. The background was a Federal Circuit decision from 1985, *In re Durden*.²⁸⁶ In *Durden*, the CAFC ruled that an old process to obtain an invention did not become new and nonobvious simply by using a new starting material or by producing a new end product. This ruling made it virtually impossible to obtain patents on biotechnology related process inventions since the general methods to produce biotechnological inventions are well known. The US PTO subsequently used the *Durden* ruling to repeatedly reject biotechnology process inventions.²⁸⁷ Seeing the damage which was done to the US biotech industry, Congress passed the Biotechnology Process Patent Protection act in 1995, amending Section 103 of the patent statute.

Another question is the impact of human genome patenting on third world countries. Developing drugs and other medical remedies is an important issue for every country. However, the fear is that less developed countries will not reap the benefits of the Human Genome Project if the patenting of human genes, and the subsequent monopoly on the exploitation of that gene, leads to higher prices on important drugs.²⁸⁸ This is especially the case if multiple licenses are needed to develop those drugs, causing the production costs to increase. Furthermore, commercial interests rather than human need motivate corporations holding patents on genes and this will determine the direction of their research.²⁸⁹ But this is not a problem isolated to drugs developed through biotechnology. It also applies to drugs developed with ordinary technology or indeed any products developed in any kind of industry. An issue which concerns the whole international patent protection system is that the countries that benefit from that system the most are those who are already the most economically powerful. This is not in the interest of the developing countries; on the contrary, it may in fact hinder the technological development of such countries. When the industrialized world holds an increasing amount of patents claiming large areas of technology, the transition to a knowledge-based society is a tough challenge for the poorer countries.²⁹⁰

6.5 Public and private interests

The research in biotechnology is basically done in two groups: academic and publicly funded laboratories on the one hand and private biotechnology and pharmacology corporations on the other. Academia typically conducts basic research, which is geared toward increasing scientific knowledge of fundamental mechanisms. This type of research is generally not directed toward the manufacture of commercially exploitable products. Biotechnology companies, on the other hand, often are more focused towards the development of commercial goods. Inventions are based on the research of many people and many of the inventions patented by corporations are thus based on the research done in publicly funded laboratories. However, in patent law, all the rewards go to the person who gets to the step of

²⁸⁶ *In re Durden*, 763 F.2d 1406, 226 USPQ 359.

²⁸⁷ www.bakerbotts.com/practice/iptech/library/articles/biotoools.html

²⁸⁸ Verma, 27 IIC 1996:3, p. 349.

²⁸⁹ Verma, 27 IIC 1996:3, p. 351.

²⁹⁰ 395 Nature 1998, p. 527.

establishing a useful invention first and the basic research that leads to that point is not compensated. Ownership in biotechnology is overwhelmingly dominated by the private sector.²⁹¹ Only 17 percent of the patents have been granted to public institutions, and most of these are US. This, in turn, is an outcome of a policy in the US encouraging public-sector researchers to apply for patents on their research results.²⁹² Furthermore, there is a well-developed collaboration between universities and industry in the US, an environment which stimulates patenting in the public sector.²⁹³ The low activity of the European public institutions when it comes to patenting biotechnological inventions is a cause for concern. If publicly funded research institutions don't file for patent protection on their findings, there is a risk of massive economic transfer from the public to the private area, since private corporations freely could use such information. One example is the patent relating to the breast cancer susceptibility gene BRCA2 by the US company Myriad Genetics. The genomic DNA sequence containing this gene was put on the Internet by two publicly funded institutions. This was rapidly exploited by Myriad, who located and cloned (purified) the gene and subsequently filed a patent covering all applications of the gene.²⁹⁴ On the other hand, many scientists in the public area believe that it is not their role to take measures towards commercialization of basic research. Many also believe that, just by reason of the fact that their research is publicly funded, it should be free for all and not be restrained by proprietary claims.²⁹⁵

6.6 Conclusions

Even if patents are generally accepted as being of great importance to the technical and economical developments in society, their consequences remain controversial in certain aspects. Too many proprietary rights might in fact be troublesome if they act to block each other. Patents on research tools used in early stages of technical innovation might therefore actually slow down the pace in research. There is no doubt, however, that national policymakers are aware of the significance that lies in an effective protection system in order to attract investment to the own industries. Both the EU Directive and the John Moore case can be seen as society's attempts to protect the national biotech industry. This, in turn, is due to the belief that biotechnology is an industry which will generate a lot of money to the national economy.

7. CONCLUDING REMARKS

Knowledge and use of human genetic information play a key role for the progress of medical science and for the future of the biotechnology industry. A healthy industry

²⁹¹ Thomas et al., 380 Nature 1996, p. 387.

²⁹² 35 USC § 200, which states: "It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development."

²⁹³ This is due to the Federal Technology Transfer Act of 1986. See further Adler 257 Science 1992, p. 910.

²⁹⁴ Thomas et al., 380 Nature 1996, p. 388.

²⁹⁵ Vogel, in Vogel and Grunwald (eds.), p. 10.

will translate to products, jobs and wealth. Growth and continued research in industry is not possible without investments. Investments will not be made unless some return is guaranteed. The question is then how inventions in the biotech industry should be protected. Given that DNA sequences are widely accepted as inventions, it can be seen as impractical to seek alternative systems of protection, such as copyright or a sui generis system. Even if the patent system was not directly designed with patents on genes in mind, it still aimed at enabling new technologies to be accounted for. Patent law has proven to be flexible enough to encompass inventions relating to genes. The patent system does not discriminate amongst inventions. In fact, inventions can be patented in all fields of technology, as is also confirmed through the TRIPs agreement. Thus, if you can characterize the gene as an invention, patent protection should be available. To obtain any patent there has to be human technical input and ingenuity. The criterion distinguishing between a discovery and an invention lies in the technical process used to identify, purify and clone the gene so as to put it to society's disposal. It must be understood that it is not the gene as present in our bodies that is patented, but a gene that is cloned outside the body. Moreover, what is needed is a disclosure of the specific function of that gene, i.e. its useful application. True scientific progress comes from the knowledge a disclosed invention brings to society. The quid pro quo for patent protection is hence the publication of the description of the invention.

While nobody owns the genes in our bodies, inventors can own the right to exploit it commercially. However, some tension between industry and research is noticeable. Scientists are concerned that there is a trend in biotechnology that seeks to control not inventions but the means of making inventions. This may result in a major shift in the strength of patent portfolios across the biotech industry. The fear is that such an outcome would impede the development of diagnostics and therapeutics, which would not be in the public interest. No doubt will public collaborations, such as the Human Genome Project, help to advance scientific knowledge. But much research is also carried out in the private sector, contributing to the development of technology. However, there is a possibility that these inventions might come at a greater cost to society due to the inherent costs of maintaining legal rights. Nonetheless, there is increasing awareness in the public domain that it needs to take part of this trend if it is to get some return of the tax funded investments. This is especially noticeable in the US. Another question is the issue of broad patent claims. There is a need to find a well-balanced scope of protection of inventions, since too broad claims can slow down progress. Such a result would be the exact opposite of the aim of the patent system. However, much debate about patent policy takes place in the absence of empirical data about the outcome and the long-term social impact.

The specific case law relating to biotechnological inventions has developed to the point where important principles have been established and clear trends have become discernible. Even though some differences still can be noticed in the three patent systems, the general trend seems to be a cautious harmonization of laws, eliminating competitive differences.

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