

THE GENETIC SEQUENCE RIGHT: A *Sui Generis* Alternative to the Patenting of Biological Materials. Luigi Palombi*

There's always a tension between those who would like to garner wealth, and they contribute a lot to society. There's also those who say, 'I believe in the common good. I want that to be enlarged.' They contribute a lot to society. The tension, the debate, between these two views is extremely important to our progress.

Prof. Sir John Sulston

PART I

The patent system¹ has at its core an exclusionary right. It is designed to exclude third parties from *making, using, vending or exercising*² the 'invention' of the patent within its jurisdiction. A patent is an asset just like any other. It can be traded. It has a value. It is property.³ Therefore, although a patent right is 'exclusionary', the 'invention' which comes within the scope of its twenty year statutory monopoly is the property of the patent owner.⁴ It belongs to the patent owner just like a piece of land belongs to the landowner.⁵ It may be an intangible asset, not real property, but trespassing upon it

Luigi Palombi LL.B., B.Ec. (University of Adelaide); Ph.D. (University of New South Wales). He was called to the Australian Federal & High Court Bar in 1982 and specialised in intellectual property law in 1986. He is presently a Consultant in biotechnology and pharmaceutical patents, a Visiting Fellow in the Faculty of Law, University of New South Wales and a Visiting Fellow of the Centre for Governance of Knowledge and Development, RegNet, Australian National University. He leads the Genetic Sequence Rights Project at ANU. He may be contacted at l.palombi@unsw.edu.au and at luigi.palombi@anu.edu.au.

Interview with ABC TV Reporter Jonathan Holmes on July 9, 2003 at the International Genetics Conference in Melbourne, Australia. Prof. Sir John Sulston is Head of the British contribution to the Human Genome Project and was awarded the Nobel Prize for Physiology or Medicine in 2002.

- ¹ There is no unitary international patent system as such. Rather, this term is used as an economical abbreviation to describe the patent systems of individual countries which today are more closely associated through various international treaties and agreements. Traditionally, patent owners either exclusively exploit the invention which is defined by a patent, or license the rights to third parties in return for the payment of certain fees, such as milestone payments and royalties. These licences can be either exclusive or non-exclusive and generally contain exploitation parameters either to geography or technology or both, so that the patent owner can control these parameters in order to maximise patent revenues. The licences may also contain terms that enable the patent owner to reach through to either own or control any improvements that may be developed by the licensee during the life of the patent. They always prohibit the licensee from challenging the validity of the patent and may require a contribution towards the payment of legal costs in the event that the validity of the relevant patent is challenged.
- ² In Australia, the exclusionary right is described as the right to 'exploit' the patent. [s.13(1) *Patent Act, 1990 AU*]. The word 'exploit' is defined to mean in respect of a product "to make, hire, sell or otherwise dispose of the product, offer to make, sell, hire or otherwise dispose of it, use or import it, or keep it for the purpose of doing any of those things."
- ³ See for example s.13(2) *Patent Act, 1990 (AU)* provides that "The exclusive rights are personal property and are capable of assignment and of devolution by law."
- ⁴ Stephen Crespi, a well known proponent of patents over biological materials argues that the term 'property' means nothing more than a farmer that owns the animals or plants that he has produced. It does not extend to ownership of a 'species' of animals, plants or organisms. He explains that "objectors draw a distinction between owning specific plants and animals and the ownership of 'whole species' which they claim is achieved by patenting. This is a clever debating point but it has no substance." See S. Crespi, *Biotechnology Patenting: The Wicked Animal Must Defend Itself*, (1995) 17(9) EIPR, 431-441. There is of course no substance in this argument. One only has to look at AU Patent 624,105 over hepatitis C virus polypeptides and nucleotides to realise that it claims do practically appropriate all HCV genotypes.
- ⁵ This analogy is imperfect. Although it must be understood that while a landowner owns a single piece of land and a patent owner owns a single invention, the way that the 'invention' is described in the patent can give him or her ownership which is much broader in scope than a single physical entity. This is because the exclusionary right applies to an intangible thing which may have application in a myriad of physical applications.

provides the patent owner with the right to unleash an arsenal of legal weaponry that includes injunctions, damages and an account of profits. Each of these weapons are designed firstly, to punish the trespasser so as to deter further trespasses and other potential trespassers and secondly, to expropriate any financial benefit received as a result of the trespass. In patent law, a trespass is called an infringement. Therefore, if any third party *makes, uses, vends or exercises* an 'invention' without the authority of the patent owner, that party will infringe the patent, just as a person who enters upon land described in a certificate of title without the authority of the landowner will trespass upon the land.

Just as landowners are not obliged to work their land, patent owners are not obliged to work their inventions. They may lock them up in vaults, never use them and exclude all others from using them for twenty years. Although compulsory licenses⁶ supposedly provide a check against this eventuality, whether these licenses are effective is another issue. For example, in Australia there has only ever been one application for a compulsory license in the entire one hundred and two year history of its patent law and that application failed.⁷

Therefore, patented inventions are the exclusive property of the patent owner. With respect to patented biological materials this means that an isolated genetic sequence of a natural gene⁸ or protein⁹ becomes the *absolute* property of the patent owner if the claim is directed to the isolated genetic sequence *per se* as a product, or the *conditional* property of the patent owner if it is directed to the isolated genetic sequence as a component in a process or method. The distinction between the absolute and the conditional is important because ownership of the absolute means that no matter how the isolated genetic sequence is used or made, patent owners can exercise their patent rights; however, the conditional means that patent owners can only exercise their rights over isolated genetic sequences in the patented processes or methods.

The absolute genetic patent claim and its consequences

An example of the *absolute* is claim 1 of Australian Patent 624,105 entitled "NANBV Diagnostics and Vaccines" granted to Chiron Corporation in 1991.¹⁰

⁶ An application for a compulsory license to use a patented invention is usually made to a court. The principal ground for the grant of a compulsory license is the non-working of the invention. See for example s.133(1) *Patents Act, 1990 (AU)* which provides that "...a person may apply to a prescribed court ... for an order requiring the patentee to grant the applicant a licence to work the patented invention."

⁷ *Fastening Supplies Pty. Ltd. v. Olin Mathieson Chemical Corporation* (1969) 119 CLR 572 (High Court of Australia, per Menzies J).

⁸ Usually described by its nucleotide sequence. There are four DNA nucleotides (bases), adenine (A), guanine (G), cytosine (C), and thymine (T). A codon is made of three nucleotides e.g., ATG, GGC, and there can only be sixty four different codons. Each codon codes for an amino acid or peptide.

⁹ Usually described by its amino acid sequence. There are only twenty amino acids, but depending on the nucleotides sequence, the polypeptides that result can be simple or complex. These twenty amino acids are common to all organisms. Polypeptides (many amino acids) are proteins.

¹⁰ This claim, incidentally, is identical to claim 1 as granted by the European Patent Office in European Patent 0,318,216, but was eventually disallowed by the Technical Appeal Board in June 2000, some eight years after grant.

A polypeptide in substantially isolated form comprising a contiguous sequence of at least 10 amino acids encoded by the genome of hepatitis C virus (HCV) and comprising an antigenic determinant, wherein HCV is characterized by (i) a positive stranded RNA genome; (ii) said genome comprising an open reading frame (ORF) encoding a polyprotein; and (iii) said polyprotein comprising an amino acid sequence having at least 40% homology to the 859 amino acid sequence in Figure 14.

This is an example of a *genetic product claim*. It gives Chiron ownership in Australia of any protein (which is what a polypeptide is) that is ‘isolated’ from its natural environment (that is, not inside a human or animal) and which is comprised (a) of at least 10 amino acids (amino acids are natural chemicals that are the building blocks of all proteins) and (b) an antigenic determinant (an antibody binding site) derived from any positive stranded RNA virus¹¹ that has ‘at least 40% homology to the 859 amino acids’ of the NS4 region (a hyper-variable non-structural region of the HCV virus genome).

While this claim does not give Chiron ownership of natural HCV *per se*, it gives Chiron ownership over specific isolated proteins that correspond to those contained in any natural HCV. Therefore, ownership of natural HCV is unnecessary because ownership over specific isolated proteins that correspond to those contained in natural HCV is good enough.

In short, the genetic products of claim 1 are nothing more than bits and pieces of naturally occurring HCV cut and spliced together in an artificial environment. While these identical bits and pieces (natural genetic components) can be brought together to form fused polypeptides which themselves do not exist in naturally occurring HCV (artificial genetic products), the natural genetic components are nevertheless individually identical to the corresponding sections of HCV genome from which they have been derived. It is important to appreciate however, that even though natural genetic components ‘can be’ used to form an artificial genetic product, they need not. In many instances the artificial genetic product is identical to and corresponds precisely with a natural genetic component and the only point of distinction is that the artificial is *isolated*¹² whereas the natural is not.¹³

¹¹ HCV is an RNA virus. Its genome is made up of a single positive stranded ribonucleic acid molecule. The molecule is made up of nucleotides contain one of four bases represented by the letters, A, G, C and U (uracil).

¹² This means that it has been removed from its natural cellular environment.

¹³ This distinction is crucial to the argument that a product of nature can be transformed into to a product of man. See the First Art. 16(c) Report of the European Commission to the European Parliament on the operation of the European Biotechnology Directive [October 7, 2002] where it states at section 4: “an element isolated from the human body, including a sequence or partial sequence of a gene, by techniques of identification, purification, characterisation and multiplication, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element. The same reasoning can obviously be applied to any element produced otherwise synthetically by a technical process.” This distinction, however, is spurious because the mere isolation of a natural gene or protein does not produce something that is substantially different to the natural. The U.S. Supreme Court in *Diamond, the Commissioner of Patents v Chakrabarty* (1980) 447 U.S. 303 only permitted the patenting of a genetically modified bacterium because it displayed “markedly different characteristics from any found in nature.” (309) The Danish Council of Bioethics in its 2004 Report entitled *Patenting Human Genes and Stem Cells* noted that “... it cannot be said with any reasonableness that a sequence or partial sequence of a gene ceases to be part of the human body merely because an identical copy of the sequence is isolated from or produced outside of the human body.” (98) See also L. Palombi, Ph.D. Thesis, *The Patenting of Biological Materials in the Context of TRIPS*, September 2004, University of New South Wales and L. Palombi *The Impact Of TRIPS On The Validity Of The European Biotechnology Directive*, Journal of International Biotechnology Law, 2005 Vol 2, 15-23.

With this type of absolute claim the application of the genetic product in any kind of technology, such as a component in an immunoassay, vaccine or anti-viral is irrelevant to the issue of infringement. The mere use of a genetic product that comes within the claim, even by a university conducting research, can amount to an infringement.¹⁴ For example, when a vaccine to HCV infection is eventually developed, if that vaccine makes use of a genetic product of claim 1, then even if it is the subject of a separate patent owned by a third party, that third party will need the authority of Chiron before it can exercise its patent rights because its patent will be subordinate to Chiron's. In fact, it is arguable that even the vaccine research conducted by that third party will itself infringe Chiron's patent if there is use of a genetic product of claim 1.¹⁵

The impact which this HCV genetic product claim had over medical and scientific research in the 1990's was explained by Prof. Baruch Blumberg¹⁶ in his testimony to the Federal Court of Australia¹⁷:

I have reviewed Chiron's Australian Patent No. 624105 [and] [i]n my opinion, the claims in this patent ... represent a view in scientific thought, i.e., that '[a]nything that is done with the HCV virus is covered by this patent and all research and development on the virus is subservient to it.' This patent essentially does not distinguish between genotype and phenotype, whereas geneticists are very aware that such a distinction should be made. It is the reductionism argument taken to the extreme and it is not supported by the great weight of the history of scientific discovery in biology and medicine. To the extent that this extreme view is backed-up by broad claims, which it is in this patent, the effect will likely be inhibition of research on HCV. Based on the unusually broad nature of the patent, if I were a research director for anti-virals and had the option of working on several viruses, the existence of this patent would weigh against my deciding to undertake HCV research. A company, or even an academic laboratory, might well be deterred from conducting research on HCV because the patent is, in effect, intimidating. With the patent as it stands, any investigator, particularly in commercial laboratories (where much of the work on hepatitis has been done) would have to seriously consider that Chiron would bring an action against them if they attempted any commercialization of anything related to HCV.¹⁸

¹⁴ See for example *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002). In its opinion, the Court of Appeals for the Federal Circuit held, "[R]egardless of whether a particular institution or entity is engaged in an endeavor for commercial gain, so long as the act is in furtherance of the alleged infringer's legitimate business and is not solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry, the act does not qualify for the very narrow and strictly limited experimental use defense. Moreover, the profit or non-profit status of the user is not determinative."

¹⁵ *Ibid.* Cf: According to the U.S. Supreme Court in *Merck KGaA v. Integra Lifesciences I, Ltd.*, 2005 U.S. LEXIS 4840 (decision June 13, 2005) even pre-clinical commercial research will come within the U.S. statutory exemption (s.271(e)(1) *Patents Act, (1952) U.S.*) provided that there is an intention to conduct those experiments with a view to ultimately seeking FDA approval.

¹⁶ Prof. Blumberg identified the causative agent of hepatitis B (HBV) in 1967. In 1976 he was awarded the *Nobel Prize for Physiology or Medicine* in recognition of his studies concerning mechanisms involved in the origin and spread of infectious diseases and, specifically, for the discovery of the hepatitis B virus and for the development of methods for detection of HBV and the vaccine for HBV. He never sought to patent HBV.

¹⁷ *Murex Diagnostics Australia Pty Ltd v Chiron Corporation* NG 106/1994 (Federal Court of Australia). There is no judgment as the case settled in week nine of the trial in August 1996 as part of a global settlement

¹⁸ *Ibid.* See the first affidavit of Prof. Baruch Blumberg filed by Murex at paras 5.1 and 5.2.

Some commentators argue that these types of statements are not supported by empirical evidence and are irrelevant because the cross-licensing of the patented technologies will overcome any obstacles.¹⁹ But these counter arguments are beside the point. Firstly, the paucity of empirical evidence is probably due to the fact that research and medical research institutions are unlikely to publish information about where their research priorities are not heading. It is more likely that they will simply divert their research towards areas where they are not hampered by patents. Secondly, if Chiron's behaviour in the early 1990's is indicative, it is noteworthy that it refused all of Murex's requests for a patent license despite that fact that Murex had patent rights to the only HCV serotyping assay in the world that enabled laboratories to detect the type of HCV infection. This was an important diagnostic tool because the only form of HCV treatment that then existed used interferon alpha alone or in combination with *ribavirin* and this treatment was effective only in some HCV patients.²⁰

The substantive point is that even if patent owners act responsibly and do license their patent rights on reasonable commercial terms, the fact that they can in their absolute discretion choose not to do so means that legally there is little, if anything, that can be done to redress the chilling effect which their behaviour and decisions have on the medical and scientific research that is covered by the patent's monopoly.

In 1999, Dr. Michael Houghton one of the 'inventors' of the HCV genetic products, admitted that after ten years of research there was no HCV vaccine.²¹ Many may see this as unexceptional admission given that vaccines generally take many decades to develop, nonetheless, Chiron made specific claims to HCV vaccines in its HCV patent application first filed with the U.S. Patent Office (USPTO) in November 1987.²² It may be that Chiron's claims to HCV vaccines did not impede vaccine research, but given Chiron's behaviour in vigorously prosecuting its HCV patent rights around the world, its refusal to license even on reasonable commercial terms and the concerns expressed by eminent scientists such as Prof. Blumberg, it is stretching credibility to suggest that Chiron's claims to HCV

¹⁹ See S. Crespi, *Biotechnology Patenting: The Wicked Animal Must Defend Itself*, (1995) 17(9) EIPR, 431-441.

²⁰ See affidavit of Dr. Peter Simmonds filed by Murex in *Murex v Chiron* NG 106/1994 (Federal Court of Australia) Dr. Simmonds testified at para 7.5 "... There is evidence that it helps determine the outcome of interferon therapy although it is unclear whether genotypes vary in their properties to cause severe liver damage [See: McComish F. *et al*, (1993) *Transfusion*, 61, Ed. H.W. Reesink D. Karger AC, Basel, 12; Okada *et al.*, (1992) *Hepatology*, 16, 619; and Tsubota, *et al*]."

²¹ "There is no vaccine for HCV and the only available treatment, IFNalpha alone or in combination with ribavirin, has proven efficacious in less than 50% of patients. Given that approximately 200 million chronic HCV infections have been estimated worldwide, there is a pressing need to develop vaccination strategies aimed at preventing and possibly eradicating HCV infection. However, several major practical and scientific problems arise in designing an HCV vaccine. First, HCV is only readily detected as RNA by PCR. Second, the only species that can be infected by HCV are humans and chimpanzees. Third, the virus does not replicate efficiently in vitro. Fourth, some viral proteins have very high mutability. Last, there is little information on correlates of immunity. Although an ideal vaccine should protect from infection, in that it should elicit sterilizing immunity, this is quite an ambitious goal in the PCR era." See Abrignani,S.; Houghton,M.; Hsu,H.H., 1999, "*Perspectives for a vaccine against hepatitis C virus*" *J. Hepatol.* 31 Suppl 1; 259 – 263.

²² Claim 64 "A vaccine for treatment of NANBV infection comprising an immunogenic polypeptide encoded within NANBV, wherein the NANBV contains a genome which encodes a polypeptide which is immunologically reactive with an antibody to a polypeptide encoded by a cDNA selected from the cDNAs in clones 5-1-1, 1-2, 81, and 91, and wherein the immunogenic polypeptide is present in a pharmacologically effective dose in a pharmaceutically effective excipient."

vaccines had no and continue to have no negative impact on scientific and medical research into HCV vaccines and treatments.

The conditional genetic patent claim and its consequences

An example of the *conditional* is claim 1 of European Patent 0,148,305 entitled “Production of Erythropoietin”²³ (Epo) granted to Kirin-Amgen, Inc. This patent expired in Europe (other than in the UK where it was held to be invalid in October 2004²⁴) in December 2004. The claim read:

A DNA sequence for use in securing expression in a procaryotic or eucaryotic host cell of a polypeptide product having at least part of the primary structural confirmation [*sic*] of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and to increase hemoglobin [*sic*] synthesis or iron uptake, said DNA sequence selected from the group consisting of:

- (a) the DNA sequences set out in Tables V and VI or their complementary strands;
- (b) DNA sequences which hybridize under stringent conditions to the protein coding regions of the DNA sequences defined in (a) or fragments thereof; and
- (c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) and (b).

This is an example of a *genetic process claim*. It gave Kirin-Amgen ownership to the use of the human erythropoietin gene (Epo gene) in a specific process, namely the use of host cells (for example, *E.coli*, *chinese hamster*) into which the Epo gene DNA²⁵ was cut and spliced so as to have the host cells express or produce Epo, a human protein.

Therefore, although Kirin-Amgen did not own the human erythropoietin gene *per se*, it owned a process²⁶ for the recombinant production of a recombinant Epo (rEpo), a substance that was identical to the natural human Epo (uEpo).²⁷ However, in Kirin-Amgen’s opinion, ownership of the process was as good as ownership of the natural Epo gene because the product of the process, rEpo, was identical to the product of the natural Epo gene, uEpo.

²³ Epo is a hormone that is produced naturally in humans and regulates the level of red blood cells. Its principle source of production is the kidneys and people that suffer from kidney failure benefit from therapeutic treatment with Epo.

²⁴ This claim was held to be invalid by the Appellate Committee of the House of Lords, some six weeks before the patent was due to expire in December 2004. See *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2004] All ER (D) 286 (UK House of Lords).

²⁵ Genes are located on chromosomes in the nucleus of a cell and are made of deoxyribonucleic acid (“DNA”). DNA is composed of two strands of nucleotides in double helix formation. The nucleotides contain one of four bases, adenine (A), guanine (G), cytosine (C), and thymine (T), that are linked by hydrogen bonds to form complementary base pairs (i.e., A-T and G-C).

²⁶ See *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2002] RPC 31 (UK Court of Appeal). In its decision (this part was upheld by the House of Lords) the Court of Appeal held that the Kirin-Amgen invention did not capture the production of erythropoietin howsoever made and that therefore the erythropoietin manufactured by Transkaryotic Therapies Inc did not infringe the patent. The Court of Appeal rejected Kirin-Amgen’s submission that the claim covered all processes for the recombinant production of erythropoietin.

²⁷ *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2004] All ER (D) 286 (UK House of Lords) per Lord Hoffmann, para 96; Also see *Amgen, Inc v Chugai Pharmaceutical Co and Genetics Institute, Inc* (1989) 13 U.S.P.Q.2D 1737 (U.S. District Court for the District of Massachusetts).

In Kirin-Amgen's U.K. litigation against Roche Diagnostics GmbH and Transkaryotic Therapies Inc (TKT) it maintained all the way to the House of Lords, that its patent covered all processes and methods of rEpo production because the disclosure of the genetic sequence of the Epo gene was the underlying piece of information that was central to the production of rEpo howsoever made. It argued that its claim, even though it was to a process, was an absolute claim to rEpo *per se* because the *end product* of the process was rEpo.

Kirin-Amgen's argument was so persuasive that Neuberger J, the trial judge, agreed. In his opinion, even though the DNA sequence of the Epo gene was a 'discovery' it was an "essential feature" of the 'invention' because it "made a technical contribution".²⁸ In other words, the DNA sequence of the human Epo gene was an 'invention' because it made the production of rEpo possible. The fact that rEpo and uEpo were indistinguishable products either physically, genetically and biologically was irrelevant to both Kirin-Amgen and the trial judge. He explained that he was "comforted" in his ruling by the fact that "over the past 20 years or so, it has been the regular practice of the European Patent Office (and, I think, of the US Patent Office) to grant claims substantially in the form of Claim 1."²⁹

The Appellate Committee³⁰ of the House of Lords, however, was not so comforted nor persuaded. Lord Hoffmann, who delivered the unanimous speech of the Committee disagreed that the invention was to rEpo howsoever produced. In the Committee's opinion, this was not possible because such a claim would be a claim to a 'discovery' *per se*.³¹ Lord Hoffmann explained that "an invention is a practical product or process, not information about the natural world ...[and] it cannot be right to give him a monopoly of the use of the information as such."³² It was therefore wrong to permit Kirin-Amgen to monopolise the production of rEpo because that would have been tantamount to transforming the DNA sequence of the Epo gene, being a product of nature, into an *invention*, being a product of man. In the Committee's opinion, the process of claim 1 was restricted to that which the claim described, namely a process that used a 'host cell'. The *invention* was the specific process, not the isolated Epo gene.

Even so, the Committee held the claims challenged in the suit³³ to be invalid because the *end product* of that process, rEpo, was indistinguishable from uEpo, a natural product that was known to exist before

²⁸ *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2002] RPC 1 (Patents Court), para 540. "Claim 1 is to a DNA sequence which is 'suitable for' the claimed purposes, and I accept Mr Waugh's submission [Kirin-Amgen's counsel] that it is 'plainly the application of the discovery which is capable of industrial application (whatever the origin of the DNA sequence)'. Per Neuberger J, para 540.

²⁹ *Ibid.*, para 541.

³⁰ The Lords Hoffmann, Hope of Craighead, Rodger of Earlsferry, Brown of Eaton-under-Heywood and Walker of Gestingthorpe.

³¹ *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2004] All ER (D) 286 (UK House of Lords) per Lord Hoffmann, para 76.

³² *Ibid.*, para 77.

³³ The challenged claims were 19, 20, 21, 22, 23, 24, 25, 26, 29 and 31 ("the dependent claims"). Each of these was held to be invalid. Claim 1, the parent of the claims dependent claims, however, was not challenged and so their Lordships did

the date of the patent application. In other words, despite the fact that the specific process was the *invention*, it was not a *patentable invention*, because even though the process was artificial, the product of the process was a substance that was identical to a product of nature.

The ruling, however, made little if any impact upon Kirin-Amgen because it came at the very end of the twenty year monopoly. Arguably, the position which Kirin-Amgen adopted and which found favour with the trial judge (and the EPO) probably encouraged many European biotechnology companies to keep clear of the production of rEpo and the development of alternative processes for its production. Whether this was a good thing for European biotechnology is unquantifiable, but what is quantifiable is extra cost that this illegal monopoly (at least in the opinion of the House of Lords) placed upon the health care budgets of European countries to which this patent applied. Even without having done the calculations it is reasonable to infer that the price of rEpo would have been higher with this patent than without it.

What is particularly concerning is that in granting this European patent to Kirin-Amgen the EPO effectively gave ownership of *information about the natural world* (using the rationale that ‘isolated’ biological materials are ‘inventions’) to a corporation that was then able to dictate, by effect of law, how that information could be used in Europe for a period of twenty years. Clearly, the House of Lords found this idea repugnant, but its rejection merely echoed the objections that were first raised by the U.K. Court of Appeal in 1988 in the *Genentech* appeal.³⁴

Interestingly, the EPO upheld the validity of this patent all the way through the opposition process from grant to the final appellate hearing before the Technical Board of Appeal (TBA). The TBA, so it seemed, was unable to grasp the point which the House of Lords saw as obvious. With diplomacy Lord Hoffmann explained away the discrepancy in results by pointing out that the TBA had found that there was a physical difference³⁵ between rEpo and uEpo and this distinguished rEpo from uEpo so as to not be identical to the natural product.³⁶ Even so, he expressed “being a little puzzled by these findings”.³⁷

Lord Hoffmann was perfectly justified in being “puzzled” because the evidence of the similarity of the two products, one artificial and the other natural, had been clearly recorded in a 1989 decision of the

not rule on the validity of this claim. Nevertheless, it is likely that it been challenged and had they therefore been in a position to rule on it that they would have also held it, and the entire patent, to be invalid (see para 132).

³⁴ *Genentech Inc's Patent* [1989] RPC 147.

³⁵ “The Board is on the evidence prepared to presume that the limitation to the polypeptide being a product makeable using the DNA of Claim 1 is a technical feature which ensures that it has a glycosylation pattern different from the known uEPO.” The TBA as quoted by Lord Hoffmann, *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2004] All ER (D) 286 (UK House of Lords), para 94.

³⁶ Per Lord Hoffmann, *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2004] All ER (D) 286 (UK House of Lords), paras 93-95.

³⁷ *Ibid*, para 95.

U.S. District Court for the District of Massachusetts in *Amgen, Inc v Chugai Pharmaceutical Co and Genetics Institute, Inc.*³⁸ There the District Court held,

...the *overwhelming* evidence, including Amgen's own admissions, establishes that uEPO and rEPO are the same product. The EPO gene used to produce rEPO is the same EPO gene as the human body uses to produce uEPO. The amino acid sequences of human uEPO and rEPO are identical. There are no known differences between the secondary structure of rEPO produced in a CHO cell and EPO produced in a human kidney. ... Amgen's own scientists have concluded that by all criteria examined, rEPO is the 'equivalent to the natural hormone.' In particular, they noted that the uEPO preparation had an equivalent biological activity in the RIA and bioassays. Amgen's Product License Application to the FDA states that all 'physical tests performed on both r-HuEPO and u-HuEPO ... show these proteins to be indistinguishable'; that r-HuEPO and u-HuEPO are 'indistinguishable in their biological and immunological properties'; and that testing 'confirms the similarity of the secondary and tertiary protein structures of r-HuEPO and u-HuEPO as predicted by the equivalence of their immunological and biological activities.

Given this decision, which was publicly available and accessible by the EPO and the TBA, the decision of the TBA cannot be as easily explained away as Lord Hoffmann diplomatically did. The lack of a full and proper explanation for the divergence of result suggests that the lack of independence of the TBA from the EPO may have influenced the TBA, especially in view of the fact that, as discussed below, (a) the EPO had been a party to the 1988 joint communiqué and (b) the EPO was a proactive supporter of the European Biotechnology Directive.

It needs to be understood that the TBA is not a truly independent tribunal and therefore there resides within the EPO opposition process, as established by the European Patent Convention of 1973 (EPC), a conflict of interest. Apart from the fact that the TBA is not a judicial body, its close association with the EPO must mean that the policy of the EPO is influential, to some degree, and from that it is fair to infer that the TBA was effected by EPO policy in reaching the decision that it did in the Kirin-Amgen opposition. Clearly, the TBA was prepared to come to a finding of fact that was at odds with the evidence in order to come to a decision that was sympathetic with EPO policy.

The European Biotechnology Directive

The *European Biotechnology Directive*³⁹ (the Directive) was passed in 1998 by the European Parliament. The Directive became law principally at the urging of the European biotechnology industry. The question which must be asked is: why was the Directive necessary if pre-Directive European patent law permitted the grant of the types of patents discussed earlier?

³⁸ *Amgen, Inc v Chugai Pharmaceutical Co and Genetics Institute, Inc* (1989) 13 U.S.P.Q.2D 1737 (U.S. District Court for the District of Massachusetts).

³⁹ Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the *Legal Protection of Biotechnological Inventions*. Official Journal L 213, July 30, 1998, 13 - 21.

The answer is simple. The patent cognoscenti had known for some time there was a problem and so as early as 1988 the EPO, the USPTO and the Japanese Patent Office (JPO) had issued a joint communiqué which stated:

Purified natural products are not regarded under any of the three laws [US, EU and Japan] as products of nature or discoveries because they do not in fact exist in nature in an isolated form. Rather, they are regarded for patent purposes as biologically active substances or chemical compounds and eligible for patenting on the same basis as other chemical compounds.⁴⁰

It is not clear what event triggered this action, but it is noteworthy that a number of biotech patent cases were brewing in the mid to late eighties and that *Genentech* was one of them. That case concerned a patent granted to Genentech Inc, at the time a relatively new biotech company. The invention was isolated human tissue plasminogen activator (t-PA), a protein which occurs naturally in humans in very small quantities, and the recombinant production of t-PA. t-PA activates the conversion of existing precursor plasminogen into plasmin, an enzyme capable of dissolving fibrin in blood clots.⁴¹ The Court of Appeal's decision in October 1988 was unfavourable to Genentech. The patent was held to be invalid for a number of reasons, one of them being that isolated t-PA was not an 'invention'. The impact of the decision was felt throughout Europe because the applicable UK patent legislation was consistent with the EPC.

Whether it was a mere coincidence that in 1988 the EPO, USPTO and JPO issued their joint communiqué, or whether it was in response to this decision, or even in anticipation of it, is immaterial. What is material is that firstly, the UK Court of Appeal disagreed with its central rationale and secondly, under the EPC it is the exclusive role of the national courts to decide patent validity in a revocation action, not the role of the European Patent Office to preempt them.

Undoubtedly, the Court of Appeal's decision in *Genentech* sent a chill down the collective spines of European patent agents, the CEO's of European biotechnology companies and the technocrats at the European Commission in Brussels (EC), for soon thereafter the EC initiated the process which led to the Directive. Indeed one of the principle architects of the Directive, Dominique Vandergheynst,⁴² explained that the Directive was a "true revolution ... between the ethical dimension and a technological sector of which certain aspects cannot but arouse control by public powers."⁴³

⁴⁰ 1988 Joint Statement of USPTO, EPO and JPO. See footnote 9, Nuffield Council of Bioethics Discussion Paper, *The Ethics of Patenting DNA*, (2002) 26, 3.14.

⁴¹ *Genentech Inc's Patent* [1989] RPC 147.

⁴² Former Responsible Official at the European Commission from 1990 to 1999 for the European Biotechnology Directive – see Foreword, in G. Kamstra et al, *Patents on Biotechnological Inventions: The E.C. Directive*, London, Sweet & Maxwell, 2002.

⁴³ *Ibid.*

The Directive took ten years and two attempts by the EC to become law. The first attempt in the mid-nineties failed. However, the EC persisted and eventually a compromise was reached between the various factions within the European Parliament.

The Directive is a revealing document because its two principle articles, art. 3⁴⁴ and art. 5,⁴⁵ expose the very weakness which the EPO tried to address with the 1988 joint communiqué. Ironically, in trying to strengthen the European patent system to cater to biotechnology, the European Parliament through the actions of the EPO and European Commission (EC) highlighted the very problem.⁴⁶

The Directive provides that ‘biological materials’⁴⁷ derived from *any natural source* including ‘elements’ from the human body that are either ‘isolated’⁴⁸ or ‘produced by means of a technical process’⁴⁹ even those identical to the ‘natural’ elements are presumed to be ‘inventions.’ The term, ‘biological materials’ as defined by the Directive include, but are not limited to, such things as viral, plant, animal and human proteins and genetic materials that code for them.

The Directive therefore reverses the impact of the Court of Appeal decision in the *Genentech* decision insofar as the ‘invention’ requirement of patentability is concerned. Patents granted by the EPO with respect to such Directive ‘inventions’ after July 2000 can only be revoked if they fail to meet the thresholds of the remaining patentability conditions which include novelty, inventive step and industrial applicability.

In other words, according to the reasoning of the Court of Appeal in *Genentech*, pre-July 2000 European patents that claim inventions over isolated or purified genetic sequences and the process or methods of production of the corresponding natural proteins are invalid. This was reinforced by the House of Lords in *Kirin-Amgen* which held that even though the primary claim was to “a perfectly

⁴⁴ Article 3.1 “... a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.”

Article 3.2. “Biological material which is isolated from its natural environment or produced by means of a technical process ... even if it previously occurred in nature.”

⁴⁵ Article 5.2 “An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.”

⁴⁶ “The European Parliament and Council directive 98/44/EC ... was crucial in order to foster the innovation and provide European companies *with adequate protection of their domestic market.*” (emphasis added) per Philippe Busquin and Frits Bolkestein of the European Commission in their foreword to the EC Report entitled, *Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation*, 2004, EUR 21122.

⁴⁷ Art. 2.1. *Directive* defines ‘biological material’ to mean “any material containing genetic information and capable of reproducing itself or being reproduced in a biological system.”

⁴⁸ This word ‘isolated’ in this context means that the biological material or human element has been separated or removed from its natural environment and has been purified to some degree.

⁴⁹ A technical process includes the process for the recombinant production of a protein.

good and ground-breaking process for making [Epo] and its analogues, [Amgen] were determined to try to patent the protein itself, notwithstanding that, *even when isolated*, it was not *new*".⁵⁰

Clearly, the House of Lords was not prepared to accept that the isolation of the Epo gene nor the elucidation of the genetic sequences of the Epo gene and Epo made any difference to what it was and its ruling therefore contradicted the 1988 joint communiqué. In other words, the isolation of the Epo gene and the elucidation of its nucleotide sequence did not *turn a pig's ear into a silk purse*.⁵¹

But the law changed with the Directive so that from July 2000 'isolated' biological materials and those produced by technical means are presumed to be 'inventions'. Even the Court of Appeal in *Kirin-Amgen*, which was considering a pre-Directive patent, was influenced by the Directive.⁵² However, as the House of Lords overruled it, whatever reliance the Court of Appeal placed on the Directive was obviously misplaced. But for post-Directive biotechnology patents, the Court of Appeal's comments suggest that the European biotechnology industry may have finally fixed the problem which the 1988 joint communiqué sought to address.

Unfortunately, the EC's solution may not be legitimate.⁵³ The uncertainty surrounding its legitimacy stems from its inconsistency with art. 27.1 of the *Agreement on Trade Related Aspects of Intellectual Property* (TRIPS). TRIPS is one of the key agreements binding all one hundred and forty six member countries and the European Community (as a separate member) to the Agreements of the World Trade Organisation (WTO). It is a requirement of the World Trade Agreement that all WTO members "ensure the conformity of [their] laws, regulations and administrative procedures with [their] obligations as provided in the annexed Agreements."⁵⁴ TRIPS is one of the 'annexed Agreements'.

Art. 27.1 TRIPS provides as follows:

... patents shall be available for *any inventions*, whether products or processes, in all fields of technology, *provided that they are new, involve an inventive step and are capable of industrial application* [and] ... *patents shall be available and patent rights enjoyable without discrimination*

⁵⁰ *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others* [2004] All ER (D) 286 per Lord Hoffmann, para 132. (Emphasis added)

⁵¹ The scepticism expressed by the House of Lords to the distinction between a natural human protein and an isolated human protein was also expressed by the Danish Council of Ethics in their 2004 Report entitled *Patenting Human Genes and Stem Cells*. At page 98 they state, "In the members' view, it cannot be said with any reasonableness that a sequence or partial sequence of a gene ceases to be part of the human body merely because an identical copy of the sequence is isolated from or produced outside of the human body."

⁵² "We draw comfort from the Directive which allows claims to biological elements 'isolated ... or otherwise produced by means of a technical process even if the structure of that element is identical to that of a natural element': *Kirin-Amgen v Hoechst Marion Roussel Ltd and others* [2003] RPC 31 at para 57 page 34 (UK Court of Appeal). (Emphasis added)

⁵³ See *The Netherlands (supported by Italy and another) v European Parliament and another (supported by the European Commission)* [2002] All ER (EC) 97 (Court of Justice of the European Communities). In this case the Court of Justice held that the Directive did not violate art. 27(3)(b) TRIPS, but it left open the issue of whether it violated other aspects of TRIPS. It held, "... the legality of a Community instrument can be called in to question on grounds of breach of international agreements to which the Community is a party ... if the provisions of those agreements have *direct effect*." The Community is firstly a party to the WTO and therefore TRIPS and secondly, art. 27.1 has a direct effect on the Community.

⁵⁴ Art. XVI.4 World Trade Agreement, 1995.

as to the place of invention, *the field of technology* and whether products are imported or locally produced.

Art 27.1 TRIPS concerns patents. It stipulates that there are four conditions of patentability. The first is the *invention*. This is a prerequisite condition of patentability because unless something is an ‘invention’ the subsidiary conditions of patentability are irrelevant. The second is the *novelty* of the ‘invention’. The third is the *inventive step* of the ‘invention’. The fourth is the *industrial applicability* of the ‘invention’. This means that each of these parameters must be satisfied before any WTO member may grant a patent, or enable one to ‘be available’ under its national patent laws. It also requires the administrative and regulatory patent regimes of WTO members to be applied and interpreted consistently with these parameters. A granted patent that does not satisfy these parameters violates TRIPS and, as a consequence, the patent law and regime from which it derives its legal status also violates the World Trade Agreement.⁵⁵ Furthermore, it stipulates that these conditions shall apply to all patents “without discrimination as to ... the field of technology”.

It is important at this juncture to appreciate that the word ‘invention’ in TRIPS cannot mean whatever a WTO member deems it to mean. While every WTO member has the power to pass whatever law its governmental system permits and therefore to define ‘invention’ to mean whatever the parliament may like, under the terms of the agreements which establish and regulate the WTO, they are obliged to conform to the terms of those agreements. This means that from January 1995, when the European Communities joined the WTO, the legislative freedoms that formerly applied to the EC and the European Parliament changed dramatically. No longer was the EC and the European Parliament able to manoeuvre European patent law as easily as the European Patent Office had tried to do in the 1988 joint communiqué. Therefore, it follows that if the Directive was not a ‘mere clarification’ of European patent law as it stood before July 2000, then arguably it represented a significant variation from that law. The extent of that variation is the contrast between the UK court decisions in *Genentech* and *Kirin-Amgen* and the 1988 joint communiqué.

While TRIPS does not provide a definition of the word ‘invention’, the lack of a definition does not mean that anything made by man is an ‘invention’. There are limits and one of the most significant limitations was restated by the U.S. Supreme Court in 1980 in *Diamond v Chakrabarty* where the Court held:

The laws of nature, physical phenomena, and abstract ideas have been held not patentable. See *Parker v. Flook*, 437 U.S. 584 (1978); *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972); *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948); *O'Reilly v. Morse*, 15 How. 62, 112-121 (1854); *Le Roy v. Tatham*, 14 How. 156, 175 (1853). Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton

⁵⁵ “Each Member shall ensure the conformity of its laws, regulations and administrative procedures with its obligations as provided in the annexed Agreements”.

have patented the law of gravity. Such discoveries are ‘manifestations of ... nature, free to all men and reserved exclusively to none.’ *Funk, supra*, at 130.⁵⁶

Accordingly, it is suggested that because (a) the Directive circumvents the necessity for biological materials to be ‘inventions’ *within the meaning of that word in TRIPS* when TRIPS mandates that all patents must only concern ‘inventions’ and (b) the circumvention itself positively discriminates *in favour* of biotechnology, that there is a plausible argument that the Directive violates TRIPS.⁵⁷

Interestingly, the EC has recently turned its attention to the potential conflict between the Directive and TRIPS. In a Report it released in 2004 entitled, *Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation*⁵⁸ Philippe Busquin, Research Commissioner and Frits Bolkestein, Internal Market Commissioner of the EC noted in their foreword:

The European Parliament and Council directive 98/44/EC of 6th July 1998 on the legal protection of biotechnological inventions came into place almost a decade after its first draft had been proposed by the Commission. *This piece of legislation was crucial in order to foster the innovation and provide European companies with adequate protection in their domestic market.*⁵⁹

At this time, some seven years since it was passed, four countries⁶⁰ of the European Communities have refused to transform the Directive into their domestic patent law. Given that both Commissioners accepted that the Directive was “crucial” to providing the European biotechnology industry “with adequate protection in their domestic market”, the obvious question is: why has it not been fully embraced in Europe?

This EC Report⁶¹ documented the discussions of an expert group⁶² that met in March 2003 to discuss the impact of the Directive as required by art. 16c. This article of the Directive requires the EC “to

⁵⁶ *Diamond, the Commissioner of Patents v Chakrabarty* (1980) 447 U.S. 303, 309 (US Supreme Court). For a complete explanation see L. Palombi, Ph.D. Thesis, *The Patenting of Biological Materials in the Context of TRIPS*, September 2004.

⁵⁷ See also L. Palombi, *The Impact of TRIPS on the Validity of the European Biotechnology Directive*, *Journal of International Biotechnology Law*, 2005, Vol 2, 15-23.

⁵⁸ European Commission Report EUR 21122, December 2004, *Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation*.

⁵⁹ *Ibid.* (Emphasis added) Also the invalidity of the Directive was foreshadowed by the Court of Justice of the European Communities in *The Netherlands v European Parliament*,⁵⁹ [2002] All ER (EC) 97 which held that, “... the legality of a Community instrument can be called in to question on grounds of breach of international agreements to which the Community is a party ... if the provisions of those agreements have *direct effect*.”⁵⁹ There can be no doubt that art. 27.1 TRIPS has a ‘direct effect’⁵⁹ on the *EPC* and the *Directive*, which are both Community instruments. In that case the validity of the Directive was challenged on the basis of alleged inconsistency with art. 27.3 TRIPS. The Court of Justice there held that the Directive was not invalid because art. 27.3 was not mandatory, but voluntary. The same, however, cannot be said of art. 27.1 where the language is unambiguously mandatory.

⁶⁰ As at the present time (October 2005) Italy, Luxemburg, Lithuania and Latvia refuse to transform the Directive. As at October 2004 this list of countries also included Austria, Belgium, Cyprus, Germany, Estonia, the Netherlands and Slovenia.

⁶¹ The Report, *Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation* (European Commission Report EUR 21122, December 2004) was written by Prof. Sven Bostyn who is not only a member of the Faculty of Law, University of Amsterdam, but also is Legal Counsel to a Belgian patent agent firm, De Clercq Brants & Partners.

monitor ‘the impact of patent law on biotechnology and genetic engineering’ and provide annual reports (‘16c reports’).⁶³ So although this particular Report is not an art. 16c Report, it is a document that was created as part of the process leading to the second art. 16c Report which was released on July 14, 2005.⁶⁴ Accordingly, the statements contained in the Report are relevant to this discussion because the expert group was established specifically to “advise the Commission on the preparation of future 16c Reports through the examination of important issues relating to biotechnological inventions.”⁶⁵

In this Report Prof. Bostyn, the author, explained that a major issue under European patent law is the “distinction between patentable inventions and non-patentable discoveries”⁶⁶ and that the requirement that the ‘invention’ be technical in nature has made the threshold of patentability “problematic” in biotechnology “especially in view of the fact that it is *very difficult* to define what technical means”.⁶⁷ Not content to leave the discussion to European patent law, he proceeded to discuss the issue of ‘invention’ under US patent law⁶⁸ explaining that even there the legal position was uncertain, although he suggested that the absence of a ‘technical’ requirement provided “the advantage of clarity”.⁶⁹

Despite the stated uncertainty of the law regarding the invention condition of patentability he confidently asserted that DNA coding for industrially useful expression products; genes as diagnostic tools and genes which control biological pathways are ‘inventions’.⁷⁰ He confirmed that the Directive made it clear that the only exception is the human body which cannot be patented under any circumstances⁷¹ and specified that a “specific [human] DNA sequence without more” is not an ‘invention’.⁷²

⁶² The expert group was made up of Ms. Anne McLaren (Wellcome CRC Institute, University of Cambridge); Ms. Stobhan Yeats (Director, Biotechnology Directorate, European Patent Office); Mr. Jacques Warcoï (Patent Agent, Cabinet Regimbeau); Mr. Daniel Alexander (Barrister, London); Mr. Bo Hammer Jensen (Director, Senior Patent Counsel, Novozymes A/S); Mr. Francisco Bernardo Noriega (Deputy Director, Intellectual Property, PharmaMar S.A.); Prof. Joseph Straus (Managing Director, Max Planck Institute for Intellectual Property); Mr. Francis Queitier (Genoscope); Mr. Ingvar Koch (Director, Patent Law Directorate, European Patent Office); and Mr. Kjeldgaard (Senior Counsellor, Biotechnology and Genetic Resources, WIPO). It is noteworthy that the majority of the members of the expert group came from either the biotechnology industry, the European Patent Office, European patent agents and WIPO, all of whom have a vested interest in maintaining the patent system.

⁶³ Foreword in European Commission Report EUR 21122, December 2004, *Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation*.

⁶⁴ Report From The Commission To The Council And The European Parliament, *Development and implications of patent law in the field of biotechnology and genetic engineering*, COM(2005) 312 final, July 14, 2005.

⁶⁵ The second art.16c EC Report specifically refers to the expert group and their deliberations at heading 1.2 page 2.

⁶⁶ European Commission Report EUR 21122, December 2004, *Patenting DNA sequences (polynucleotides) and scope of protection in the European Union: an evaluation*., at heading 3.3 page 12.

⁶⁷ *Ibid.* (Emphasis added).

⁶⁸ *Ibid.*, pages 13-14.

⁶⁹ *Ibid.*, page 14.

⁷⁰ *Ibid.*, pages 38-39.

⁷¹ *Ibid.*, page 40.

⁷² *Ibid.* He also refers to recital 16 of the Directive which states that “the simple discovery of one of [the human body’s] elements or one of its products, including the sequence or partial of a human gene, cannot be patented.”

Then he made the usual intellectual leap, consistent with the 1988 joint communiqué, that the isolation of a genetic sequence from its natural environment is an ‘invention’ because it has been so removed “via a reproducible technical process” which involves the making of a “selection in the sequence” and the production of cDNA⁷³ “which does not occur as such in nature”.⁷⁴ He concluded therefore that the Directive was a ‘mere clarification’ of European patent law.⁷⁵ But in doing so, he focused only on the practice of the EPO and completely ignored the UK Court of Appeal decision in *Genentech*.

Finally he arrived at the crucial issue – art. 27.1 TRIPS. Although he limited his discussion to the discrimination prohibition in art. 27.1 TRIPS and acknowledged that “it could be argued that TRIPS does not allow discrimination as to the field of technology for which patent protection must be available” he suggested that in the absence of any “uniform interpretation” of art. 27.1 TRIPS that “member states can determine the type of protection they provide.”⁷⁶

His argument that there can be disparity in the patentability thresholds between WTO members provided that the four conditions of patentability are incorporated into domestic patent law, however failed to take the fundamental objectives of TRIPS which is to “reduce distortions and impediments to international trade” and to “promote effective and adequate protection of intellectual property rights”.⁷⁷

Enabling WTO members to individually “determine the type of protection they provide” detracts from, rather than enhances, *the effective and adequate protection of intellectual property rights* because once the thresholds to the patentability conditions in art. 27.1 TRIPS need not meet a set of uniform standards they become meaningless. It suggests that something that can be an ‘invention’ according to the patent laws of one WTO member may not be according to the patent laws of another. Seriously, if that were the case, art. 27.1 TRIPS would be otiose.

PART II

The nub of the problem for biotechnology is the simple fact that much of the commercial value of its intellectual property resides in the production of recombinant proteins that merely replicate the function or performance of natural proteins. It is the *in vivo* identity that is valuable but it is this which cuts across the prohibition against the patenting of “laws of nature, physical phenomena, and abstract ideas” as restated in *Chakrabarty*.

⁷³ cDNA means copy DNA.

⁷⁴ *Ibid*, page 41.

⁷⁵ *Ibid*, Heading 4.6.2 page 53.

⁷⁶ *Ibid*, page 66.

⁷⁷ “Desiring to reduce distortions and impediments to international trade, and taking into account the need to promote effective and adequate protection of intellectual property rights, and to ensure that measures and procedures to enforce intellectual property rights do not themselves become barriers to legitimate trade.”

It is important to appreciate that not only are the recombinant proteins produced by the processes not substantially different to natural proteins, but neither are the isolated genetic materials used in those processes. The genetic components and the end products of these processes are therefore indistinguishable from the natural and, as has been long recognised by *Chakrabarty* and *Genentech* and most recently by *Kirin-Amgen* they are not ‘inventions’. This must mean that the patent system cannot provide the level of intellectual property protection that the biotechnology industry seems to demand. Critically though, it means that the creativity, ingenuity and invention which an efficient patent system should nurture and encourage is being undermined by the grant of patents that are creating patent thickets so dense⁷⁸ that they are adding unnecessary costs to medical and scientific research and, in some instances, hindering it altogether.⁷⁹

Stephen Crespi has explained that “the word ‘invented’ sounds strained when applied to something already existing.”⁸⁰ Of course he is right, because it is impossible to invent something that already exists, even if its existence is unknown. But, to suggest, as he does that “the word ‘discovered’ ... glosses over the painstaking work that has to be done by the scientist before he can see the pure substance in the test tube,”⁸¹ and that therefore ‘isolation’ is a legitimate device to transform a product of nature (i.e., a ‘discovery’) into a product of man (i.e., something capable of being an ‘invention’) is an attempt to distort the patent system. True it is that the word ‘discovery’ glosses over “the painstaking work that has to be done by the scientist,” but the threshold of invention is not ‘painstaking work’. If that were the case, then literally anything ‘made by man’ could be considered to be an ‘invention’. The simple truth is, that like it or not, the ‘international’ patent system as regulated by TRIPS, requires that whatever has been the subject of ‘painstaking work’ be an ‘invention’ and if it is not, it is ineligible for patent protection.

Unfortunately, rebutting this argument does not address the fact that the ability to mass produce recombinant proteins is commercially, medically and scientifically advantageous and there can be no doubt that the isolation of genes and proteins has greatly contributed to the betterment of human health throughout the world. In these circumstances it is not only fair, but appropriate that the work that has facilitated the isolation of these proteins be rewarded, if for no other reason than that the work leading to their isolation is not only ‘painstaking’ but necessarily involves high risk investments. This is the point which Stephen Crespi and the biotechnology industry⁸² have made time and time again. Their

⁷⁸ Researchers K. Jensen and F. Murray conducted a survey of US patents granted with respect to nucleotide sequences to the human genome (i.e. genes or gene sequences). Their survey however, did not include claims to human proteins (amino acids). Even so, their results show that “nearly 20% of human genes are explicitly claimed as U.S. I.P.” which “represents 4382 of the 23,688 genes in the database of the U.S. National Center for Biotechnology Information. These genes alone represent “4270 patents within 3050 patent families” and these patents are owned by 1156 different organisations. See K. Jensen and F. Murray, *Intellectual Property Landscape of the Human Genome*, 2005, Science, Vol 310 at pages 239-240.

⁷⁹ *Op cit*, 18.

⁸⁰ S. Crespi, *Biotechnology Patenting: The Wicked Animal Must Defend Itself* (1995) 17(9) EIPR, 431-441, 432.

⁸¹ *Ibid*.

⁸² The English BioIndustry Association has argued, “the patentability of genes *per se* strikes the most appropriate balance between rewarding the inventor for their contribution to the technical field and the monopoly conferred by the patent. We

error, however, has been to stubbornly rely upon the ‘international’ patent system, rather than to advocate for a *sui generis* intellectual property right. What they have failed to accept is that the patent system has its limits and consequently biotechnology cannot be wholly served by the patent system.⁸³ Then, neither should it be.

This paper therefore proposes the creation of the Genetic Sequence Right (GSR) as a *sui generis* system of intellectual property.

Under this proposal the GSR would be administered using the existing administrative system utilised by the present ‘international’ patent system so as to minimise establishment costs and to facilitate its adoption. A GSR would be granted to the first person to file and disclose a genetic sequence defining genetic material of any origin and explaining its function and utility. A GSR would be the subject of a written application filed in the patent office of the country of application, similar to a PCT application for a patent. The GSR would become part of an international electronic database which would be freely accessible by any person.

Upon registration the GSR holder would have the right to a *GSR use fee* (GSR fee). The GSR fee would vary depending on the nature of the use. For publicly funded institutions such as universities, experimental use would not attract a GSR fee, but for commercial entities, the GSR fee would apply commensurately with the nature of the use. For example there could be scale for commercial entities starting at experimental use and moving through to full commercialisation. It is envisaged that there would be a multitude of variations in between. The amount of the GSR fee would be set by a published scale determined by a centralised world body responsible for the global administration of the GSR, for example, WIPO. This body would collect and distribute the GSR fee revenue and could earn revenue by the collection of application and annual administrations fees, as well as by retaining a small percentage of the GSR fee revenue collected. Specific allowance could also be made for GSR holders to seek GSR fees above the published scale if the GSR holder could establish that due to factors relating to the nature of the GSR or unforeseeable events (e.g., war), the total amount of GSR fees would be insufficient to recoup a fair return on the investment in the research and development leading to the GSR.

GSR users would be required to register their use with the local administrative authority and that use would be registered on the GSR electronic database. This would provide a public record of use.

The life of the GSR would be ten years from the date of registration. Infringement of GSRs could be dealt with through the relevant national courts. The holder would accordingly have the right to seek

admit that this is an imperfect balance, but we believe that this balance is more equitable than that achieved by denying *per se* patent protection for genes or other molecules.” See BioIndustry Association (UK): statement published December 21, 2001 in response to British Medical Association’s discussion paper on Gene Patenting.

⁸³ See A. McInerney, *Biotechnology: Biogen v Medeva In The House Of Lords*, (1998) 20(1) EIPR 14-21.

injunctions, declarations, or damages. Criminal provisions would also make it an offence for breaches the holder's GSR rights.

Moreover, if the GSR were to be identified through the provision of traditional, tribal or indigenous knowledge or information a portion of the GSR fee due to the GSR holder would be paid to the persons who are the owners of at knowledge or information. Their entitlement would be commensurate with the contribution made in the identification of the GSR and would be determined by the central administrative authority, which would also oversee the distribution of the GSR fee revenue to the relevant peoples.

The GSR would thereby provide a system by which investors in genetic research could be remunerated without the GSR holders having the power to control the uses to which that GSR may be put. The GSR would thereby facilitate the publication of genetic sequence information and encourage the use of genetic sequence information and the production of corresponding biological materials. However, by removing the element of absolute control, the GSR would prevent GSR holders from controlling further down-stream research or other uses.⁸⁴

The GSR holder would not need to satisfy any 'invention' or 'inventive step' criteria. Novelty of the genetic sequence could be established by a search of the GSR database or other genetic sequence databases. Novelty of the GSR could also be established by function and utility, so that even if the genetic sequence is already known or the subject of an existing GSR, establishing a novel function and utility not previously known could give rise to a new GSR. However, broad GSR description regarding function and utility would not be permitted unless substantiated throughout the breadth of the description. The GSR would therefore incorporate a description of the function and utility of the GSR.

The GSR would also address the many concerns that surrounding experimental use. One issue that is problematic with experimental use exemptions for patent infringement in the context of biotechnology, is that many patents have been granted over 'research tools' that are useful in the search for new drugs. In the context of each of these applications, the patented biological materials have been used by research institutions, such as universities, and the issue that has arisen is whether such use is or should be exempted from patent infringement.

Under the GSR, use by a teaching or research institution would be zero rated for GSR fee purposes. However, a commercial entity's use of a GSR, either directly or indirectly through a university, would attract a GSR fee commensurate with such use. The obligation to pay the GSR fee would remain with

⁸⁴ As has been amply demonstrated by the experience of health care systems throughout the world in the early 1990's with HCV diagnostics, Chiron's refusal to license competing but complementary HCV diagnostics had serious consequences. This level of control, while being appropriate for traditional types of inventions such as mechanical or engineering or electrical or even pharmaceutical in some cases, is not appropriate when the scope of the claims captures the very ingredient upon which human health was dependent. While one cannot undermine the significant benefit to humanity of the scientific work which lead to the cloning and sequencing of HCV, it needs to also be appreciated that much of the funding for that work came from public sources. It also needs to be appreciated that while significant, the information

the commercial entity. Therefore, if any commercial entity entered an agreement with a university to conduct research on its behalf or as part of a joint enterprise or collaboration, the obligation to pay the GSR fee would continue. This would remove the debate about when, and if, universities that are conducting commercially funded research should be the subject of an experimental use exemption.

The dilemma which today confronts the patent system in this regard has been illustrated most aptly in the case of *Madey v Duke University*.⁸⁵ In this case the U.S. Court of Appeals for the Federal Circuit (CAFC) considered whether the common law research exemption under US patent law applied to Duke University in respect of its use of certain equipment that was the subject of two US patents granted to Dr. Madey. The equipment had been used in a physics laboratory while Dr. Madey was associated with the University. After Dr. Madey resigned, the University continued to use this equipment without Dr. Madey's authority and he sued the University for patent infringement. On appeal to the CAFC, Dr. Madey prevailed. Crucially, the CAFC held that the University was not able to rely on the common law research exemption to patent infringement because "use in keeping with the legitimate business of the alleged infringer does not qualify for the experimental use defence".⁸⁶ The CAFC explained,

Our precedent clearly does not immunise use that is in any way commercial in nature. Similarly, our precedent does not immunise any conduct that is in keeping with the alleged infringer's legitimate business, regardless of commercial implications. For example, major research universities, such as Duke, often sanction and fund research projects with arguably no commercial application whatsoever. However, these projects unmistakably further the institution's legitimate business objectives, including educating and enlightening students and faculty participating in these projects. These projects also serve, for example, to increase the status of the institution and lure lucrative research grants, students and faculty.⁸⁷

The CAFC's reasoning essentially means that *any* use of a patented biological material or process which is related to the business of education, in the case of a university, or the business of research, in the case of a research institute, will not come within the US common law exemption to patent infringement.

Conclusion

The GSR proposal recognises that the use of genetic sequences or biological materials (that are identical to naturally occurring sequences and materials) for whatever purpose should not be controlled nor come under the ownership and control of any one organisation or person. Its purpose is to encourage third party use, rather than attempting to control or restrict it. It recognises that irrespective of whether a genetic sequence is an 'invention' or not, the elucidation of a genetic sequence and the

provided by the discovery of HCV was so fundamentally connected with human health that it was obscene to treat it like any other commodity.

⁸⁵ *Madey v Duke University* (2002) Case 01-1567 (CAFC) decision delivered October 3, 2002.

⁸⁶ *Ibid.*

⁸⁷ *Ibid.*

identification of its function is important work that should be encouraged. It therefore enables universities to fund their research projects by becoming GSR holders without incurring any obligation to pay GSR fees. It provides a system to record GSR's and assess the uses to which they are put. The fact that universities are in the business of education or, that today, see themselves as part of a broader commercial world becomes irrelevant.

Unlike the patent system which creates property in the patented invention and one which gives the patent owner the right to deal with that property as he or she sees fit, the GSR does not. Rather the GSR holder is recognised as being the first to enable the publication of new biological materials and their function and accordingly the *quid pro quo* for its disclosure is the entitlement to receive a GSR fee revenue. Accordingly, the more use of that GSR the greater the potential GSR fee revenue. Whereas with the patent system, the price of the patented invention can be subject to manipulation through the patentee's ability to control third party use. It is this ability to control and restrict use that provides the rationale for the experimental use exemption in an attempt to balance the needs of the patentee with the needs of society. However, with the GSR there is no further balancing or fine tuning required because the whole system is designed to encourage both commercial and non-commercial use equally.

This proposal is merely in its infancy. Therefore this is not the time to accept nor reject it. Rather it is time for careful reflection, suggestion and constructive criticism. After all, as Prof. Sir John Sulston said, "the tension, the debate, between those garnishing wealth and the enlargement of the common good is extremely important to our progress" and this proposal is put forward in an attempt to diffuse this tension.