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Beyond Recombinant Technology: Synthetic Biology and Patentable Subject Matter

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Even though it is not yet clear as a matter of law that isolated biological materials are indeed patentable subject matter, not only have patents over such materials continued to be granted throughout the world, but the European Parliament passed the Biotechnology Directive in 1998 in an attempt to put an end to the debate. The problem is that TRIPS requires that patents be granted for 'inventions' only and there is a real question over whether isolated biological materials or those made by the use of synthetic biology are indeed inventions within the meaning of the word in TRIPS. But technology is rapidly developing. Recently Craig Venter, the man who wanted to patent the human genome, made history again. This time he has built a synthetic bacterium from the ground up - in a laboratory. The bacterium, Mycoplasma genitalium, is a naturally occurring thing. It is the smallest known bacterium consisting of 582,970 nucleotides. Venter's version of this bacterium is identical, except that he made it. Does this make it an invention? Indeed, Venter has in mind to use this synthetic bacterium and other synthetic biological materials as vectors within which to insert genetic material that is foreign to that organism. The idea is to use these vectors to manufacture other biological materials. It's a repeat of Cohen and Boyer's idea, which they also patented, but this time, the vector itself will be a human construct. Is the patent system ready for Venter and his 'invention'?

When James I, as King of England, Ireland and France (James VI of Scotland), signed Lord Coke's *Statute of Monopolies* into law in 1624 the idea that a natural phenomenon could be a 'manner of new manufacture' would have been as repugnant to him as the idea that God did not exist. In fact so fundamental was his belief that his entitlement to reign was a sacred contract between God and himself that ultimately his son Charles I would rather die than betray his father and his maker. Indeed throughout Christendom it was understood that God created the world and everything on it and no man or woman could claim something God-made as their own on pain of ridicule, exile, excommunication or death. So it was that when Chief Justice Berger some three hundred and fifty years later declared in *Chakrabarty*, once again, that 'laws of nature, physical phenomena and abstract ideas'[1] were not patentable subject matter, he was reaching back to the very beginning of Anglo-American patent law when it was unquestioned that these "God given" things were to be 'free to all men and reserved exclusively to none.'[2]

Yet when Kyle Jensen and Fiona Murray published the results of their study, in their *Science* paper *The Intellectual Property Landscape of the Human Genome*[3], they discovered: 'nearly 20% of human genes are

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[1] *Diamond v Chakrabarty* (1980) 447 US 303, 309 citing *Parker v. Flook*, (1978) 437 U.S. 584; *Gottschalk v. Benson*, (1972) 409 U.S. 63, 67; *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, (1948) 333 U.S. 127, 130; *O'Reilly v. Morse*, (1854) 15 How. 62, 112-121; *Le Roy v. Tatham*, (1853) 14 How. 156, 175.

[2] *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, (1948) 333 U.S. 127, 130.

[3] Jensen, K. and Murray, F. (2005), 'Intellectual Property Landscape of the

explicitly claimed as US IP'.[4] Of the 23 688 human genes that made up the human genome database of the National Center for Biotechnology Information, their study revealed that 4382 of them were the subject of 4270 patents within 3050 patent families[5] and controlled by 1156 patent owners, of which 63% were private firms.[6] The largest single patent owner of some two thousand human genes was Incyte Genomics, a US corporation.

As Jordan Paradise, Lori Andrews and Timothy Holbrook, professors of intellectual property law, pointed out in their *Science* paper[7], when it comes to human gene sequences 'the "invention" is the information'[8], that is the 'invention' is information about the natural world. As a result they argue: '[g]ene patents, especially, limit what can be done in the realm of scientific research and medical care because there are no alternatives to a patented gene in diagnosis, treatment, and research.'[9] Naturally if a gene patent is to have any commercial value, it is the information about the natural world captured by the patent monopoly which underpins that value. It is this information that holds the key to the diagnosis and treatment of human genetic disease and illness because, in the final analysis, it is this which will make the 'invention' useful as a diagnostic, therapeutic or pharmaceutical. So when Amgen, Inc patented erythropoietin in 1984 it claimed as its invention a substance made artificially by the use of a recombinant gene even though, as the Federal District Court in *Amgen, Inc v Chugai Pharmaceutical Co and Genetics Institute, Inc* (1989) 13 U.S.P.Q.2D 1737 had found it was, 'the same product' as erythropoietin made by the human body. Not only that, 'the overwhelming evidence', the Court declared, proved beyond any shadow of doubt: 'the [erythropoietin] gene used to produce [recombinant erythropoietin was] the same [erythropoietin] gene as the human body uses to produce [erythropoietin] … [and] by all criteria examined, [recombinant erythropoietin was] the "equivalent to the natural hormone."'

Yet Amgen still has patent protection over isolated and purified erythropoietin as a product in the US (and will have until 2012) despite the fact that the human erythropoietin gene was isolated more than 20 years ago. Quite apart from the fact that the *quid pro quo* that an inventor supposedly pays society in return for the grant of a 20 patent monopoly is a thorough and complete description of how the invention was made so that others can make it, as Paradise, Andrews and Holbrock have concluded, 'many patents [claim] far more than what the inventor actually discovered' while others claim 'discoveries' which the patent holder has not 'specifically' described.[10] It would seem, moreover, that on the basis of the Amgen example, 20 years is the minimum not the maximum period of patent protection.

David Olson of Stanford Law School[11] mercilessly accuses the US Court of Appeals for the Federal Circuit (CAFC) of being derelict in its duty. Blaming the Court for abandoning 'any subject matter

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Human Genome', *Science*, 310 (5746), 238-240.

[4] Ibid, 239.

[5] Ibid.

[6] Ibid, 240.

[7] Paradise, J., Andrews, L. and Holbrook, T. (2005), 'Patents on Human Genes: An Analysis of Scope and Claims, *Science*, 307, 1566-1567.

[8] Ibid, 1566.

[9] Ibid.

[10] Ibid.

[11] Olson, D.S. (2006), Patentable Subject Matter: The Problem of the Absent Gatekeeper, *SSRN*, 933167.

gatekeeping role'[12], he makes the case that the result is, 'bad for society' because it means: 'patents [are] being granted in areas in which inventors do not need the incentive of monopoly grants.'[13] Olsen, of course, is not alone in his condemnation of the CAFC, nor is he the first. Arti Rai, while an Associate Professor of Law at San Diego University, blamed the CAFC's reductionism for substantially diminishing 'the balance between property rights and the public domain achieved by various patentability requirements' [14]; and before her Anita Varma and David Abrahams, themselves former USPTO patent examiners then while students at Georgetown University, expressed the view that unless the CAFC balanced, 'the needs of individual biotech patent applicants with the needs of the market', it would result in 'the stultification of technological growth'.[15] But Rai's, Varma's and Abraham's issue with the CAFC was about the obviousness standard, not the subject matter standard, which Varma and Abraham believed was 'too lax'. Indeed their argument with the CAFC was not so much about whether isolated biological materials were patentable subject matter, but whether they were obvious in light of the prior art. So the CAFC stood accused of failing to apply not only one, but two patentability standards.

Recently, though, the CAFC has been pulled up by its bootstraps. In *KSR International Co v Teleflex Inc* (2007) 127 S Ct 1727 the point in issue was over the CAFC's lowering of the obviousness threshold even further. The CAFC had held that unless a person of ordinary skill in the art was 'motivated to look at relevant prior art references', the prior art references were irrelevant in determining obviousness. The invention at the centre of this case was a mechanism that caused adjustments to motor vehicle accelerator pedals, so that irrespective of where in the car the driver was seated and the length of his leg, the driver's foot reached the pedal. In what was a close replay of *Diamond v Diehr* (1980) 101 S. Ct. 1048, here KSR had developed an adjustable pedal system for cars with cable-actuated throttles. The idea of having adjustable pedals was old and there were plenty of examples in the prior art, but KSR had modified its system by adding a modular sensor for trucks using computer-controlled throttles (like adding a computer on an old process to make an old product). Unfortunately this modification came within the scope of a patent owned by Teleflex (which had been granted on the basis of CAFC precedence in *Diehr*), and when KSR was sued for patent infringement the validity of Teleflex's patent was challenged on the grounds that the invention was obvious in light of a number of prior patents that concerned adjustable motor vehicle pedal systems.

At the trial before the District Court the evidence satisfied the trial judge that the obviousness standard had been breached and as a result Teleflex's patent was held invalid; but on appeal the CAFC reversed by ignoring two prior patents on the basis of their *motivation* test - that is, that the skilled person would not have been motivated to read them and so were not part of the relevant prior art. The CAFC held that even though the patents were about adjustable motor vehicle pedal systems, they were addressing technical problems that were different to those that Teleflex's patent addressed. In what was a classic case of shifting the goal posts, the CAFC then cited its decision in In re *Deuel* (1995) 51 F.3d 1552 to support its conclusion that 'obvious to try' was not an

[12] Ibid, 3.

[13] Ibid, 1.

[14] Rai, A. (2000), 'Addressing the Patent Gold Rush: The Role of Deference to PTO Patent Denials', USD School of Law, Public Working Paper No 5 and Law and Economics Research Paper 2, *SSRN*, 223758.

[15] Varma A. and Abraham D. (1996), 'DNA Is Different: Legal Obviousness and the Balance Between Biotech Inventors and the Market', *Harvard Journal of Law & Technology*, 9, 53.

indicia of obviousness.

The US Supreme Court, however, rejected this reasoning and in doing so sent a strong message, not only to the CAFC but to the many US patent attorneys that believed that the US Supreme Court ought to display a more 'benevolent attitude towards patents'.[16] Justice Kennedy made it clear that the Court preferred, 'the "functional approach" of *Hotchkiss*'[17], over, 'the rigid approach of the Court of Appeals'. Indeed, not only did this strike the right balance but reinforced the fact that the 'combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.'

One would think that *KSR* should have marked the end of the biotechnology patenting gold rush that had started in the late 1970s, and there are indications that the brakes are being applied. In May 2007 the United States Board of Patent Appeals and Interferences in *ex parte Kubin & Goodwin* (2007) Appeal 2007-0819, Board of Patent Appeals and Interferences (BPAI), upheld the USPTO's rejection of a patent application that claimed an invention for polynucleotides (nucleic acids) encoding Natural Killer Cell Activation Inducing Ligand polypeptides (NAIL) (amino acids), on the grounds of obviousness. The appellants had relied on the CAFC's decision in *Deuel* as authority against the USPTO's rejection. The Board, however, held that *Deuel* was 'not controlling' and, thus, '[did] not stand in the way.' In what was a clear rebuff to the CAFC's precedence, 'to the extent that *Deuel* [was] considered relevant to this case', the Board held, that the Supreme Court had 'recently cast doubt on the viability of *Deuel* to the extent the Federal Circuit rejected an "obvious to try" test.'

The fallacy in the CAFC's reasoning in *Bell* and *Deuel*[18] have finally

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[16] Karl Lutz, a practicing US patent attorney, wrote in 1953 that the, 'less than benevolent attitude towards patents' was contrary to the intent of Article I, Section 8, Clause 8 of the US Constitution, which expressly gave Congress the power, 'To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries'. In his opinion the intent had been 'mis-read' by a US Supreme Court that had limited patents, 'only for such startling innovations as [those that] "push back the frontiers of chemistry, physics, and the like" and "make a distinctive contribution to scientific knowledge"'. See Lutz, K.B. (1953), 'The New 1952 Patent Statute', *Journal of the Patent Office Society*, 35 (3), 155-162, 157 quoting Justices Douglas and Black in *Great A. & P. Tea Co. v Supermarket Co*. 71 Sup. Ct. 127. John Powell, a US patent lawyer, explained in 1959 that the legal gyration over the obviousness standard was due to, 'the statutory presumption of validity' which had become meaningless, because of: 'a judicial feeling that the Patent Office was applying a standard of invention lower than that which the courts were bound to observe and that, therefore, little if any weight could legitimately be given the presumption.' See Powell, J.F. (1959), 'Patents: Standard of Invention: Effects of Sections 103 and 282 of Patent Act of 1952', *Michigan Law Review*, 57 (3), 426-429.

[17] The obviousness condition of patentability, first established nearly a century earlier in the case of *Hotchkiss v Greenwood* (1850) 11 How. (52 US) 248 was written into the US Patents Act, 1952 in s.103. In *Hotchkiss* the US Supreme Court held that obviousness was a barrier to patentability unless the inventor could show: 'more ingenuity and skill … than were possessed by an ordinary mechanic acquainted with the business'. This squared with the generally held notion of what the act of invention required at the time. Over time however, in a seesaw of court decisions, the obviousness standard moved back and forth creating enormous scope for academic debate and disagreement and so the legislators believed that by codifying the law in s.103 of the 1952 legislation that some stability could be brought to the law.

[18] In *In re Bell* (1993) 991 F.2d 781 the USPTO and the Board of Patent Appeals had both rejected a patent application for an invention over isolated nucleic acid molecules containing human DNA that coded for human insulin-like growth factors. The issue that confronted the CAFC was:

been denounced by the US Supreme Court. Applying *KSR,* the BPAI in *Kubin* explained that the '"problem" facing those in the art', was the limited number of methodologies available to isolate NAIL cDNA, meaning that the 'skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. Thus isolating NAIL cDNA was "the product not of innovation but of ordinary skill and common sense"', and led them to conclude, 'NAIL cDNA [was] not patentable as it would have been obvious to isolate it.'

There still remains, however, the issue of patentable subject matter. The *Patents Act, 1952* made no change to the term 'composition of matter' in s.101[19] – a term that first appeared in the US patent lexicon in 1793. Without doubt the significance of this term has changed since then, but it is doubtful that it was ever intended to embrace isolated biological materials that are identical or substantial identical to products of nature. Indeed, it is arguably the case that isolated biological materials come within the express exclusion that applies to 'laws of nature, natural phenomena and abstract ideas' and, therefore, do not come within the US Constitutional mandate of Article I, Section 8, Clause 8. Not only has Rebecca Eisenberg, an American law professor, observed that US the Supreme Court in *Chakrabarty*, 'did not reach the issue of whether naturally-occurring microorganisms that have been newly isolated or purified also fall within the ambit of "manufactures" or "compositions of matter"', but the Danish Council of Bioethics has rejected, for being 'unreasonable', the idea 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.'[20]

This should come as no surprise to the scientific community who have known all along that isolation and purification merely describes the state of the thing and not what it is. In other words, if something is isolated and purified it is not different either in form, quality or property; it merely is in a different environment to that in which it is normally found or is in a purer form. For instance an orange that has been cleaned and coated with borax is no less an orange than if it had not been. In *American Fruit Growers v Brogdex* (1931) 283 US 1, in describing the Federal Court of Appeal's ruling as 'not tenable', Justice McReynolds, the author of the US Supreme Court

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'whether the … amino acid sequence of a protein in conjunction with a reference indicating a general method of cloning renders the gene prima facie obvious'. In reversing the Board's decision the CAFC held that neither, 'the prior art references, either alone or in combination, teach or suggest the claimed invention', because of, 'the degeneracy of the genetic code'. The CAFC reasoned that the, 'vast number of nucleotide sequences that might code for a specific protein' made the predictability between the genetic structure of genes and protein structure impossible and therefore not obvious. In order to provide patent protection for the biotechnology industry the CAFC accordingly moved the goal posts of 'invention' away from the techniques used to identify the human genes and towards the actual protein sequence and the gene that coded for it; and since the genetic sequence of the relevant gene had not been published, only the partial amino acid (protein sequence) of the insulin-like growth factors, it was an invention to identify and isolate the gene. Two years later the CAFC applied this reasoning in the case of *In re Deuel* (1995) 51 F.3d 1552 holding that the invention to isolated and purified DNA and cDNA (copy DNA) molecules (nucleotides) encoding heparin-binding growth factors (amino acids), was not obvious.

[19] '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 thereof, subject to the conditions and requirements of this title.' S.101 US Patents Act, 1952.

[20] Danish Council of Ethics (2004), *Report on Patenting Human Genes and Stem Cells*, 98.

opinion, made it clear that it was wrong to construe the invention as: 'a combination of the natural fruit and a boric compound carried by the rind or skin in an amount sufficient to render the fruit resistant to decay.' While it was correct to say, 'the complete article [in this form] is not found in nature', this fact alone did not make it an 'article of manufacture'. Rather an indicia of invention was whether the orange itself was, as a result of the process described in the patent, given a 'new or distinctive form, quality, or property'. In this respect, while the application of borax on the surface of the orange resulted in the orange having a longer shelf life, in truth there was 'no change in the name, appearance, or general character of the fruit'. So while the evidence established that the application of borax on the surface of the orange achieved a useful result, it did not give the patent owner the right to claim a patent monopoly over the fruit itself. That, after all, was not anyone's invention.

It is quite remarkable to believe that it could be otherwise. In fact, even P.J. Federico, the American patent scholar whose words 'anything under the sun made by man' were immortalised by the Chief Justice of the US Supreme Court in *Diamond v Chakrabarty* (1980) 447 US 303 in a footnote, admitted as much when he studied two US patents that were granted to Louis Pasteur in 1873.[21]

The first, US 135,245, was granted on 28 January 1873. Entitled 'Improvement in Brewing Beer and Ale', in one and a half pages it provided details of a process that improved 'the capacity of unchangebleness' of beer and enabled it to be 'transported without detriment or deterioration'. The second, US 141,072, was granted on 22 July 1873. Entitled 'Improvement in the Manufacture of Beer and Yeast', in a little over two pages it provided details of a process and drawings of an 'apparatus' which, when used together, would: 'eliminate and prevent the multiplication [of] … microscopic organisms … in "brewers" yeast, worts, and beer'. According to Pasteur, these 'pernicious germs' were capable of 'changing the condition of the product'. In other words, they caused beer brewed using traditional methods to spoil. His process involved the heating and cooling of the 'wort' and the use of 'pure alcohol yeast', thereby eliminating 'germs' and producing a beer that could be 'preserved without the aid of ice' and 'made in hot as well as cold climates, as summer as in winter.'

The function of yeast in the brewing process, as Pasteur had discovered while studying the fermentation process in wine in the 1850s, was to convert sugars into alcohol using what he called 'ferments'.[22] Applying this discovery, Pasteur went on to develop a process that improved the quality of beer but, inexplicably, in patenting his invention he never claimed his improved beer as an 'invention'. True, beer was not a new product and could not be patented as such; but given that the beer brewed using his patented processes had a longer shelf life, could be transported without loss of quality and could be made all year round, attributes that traditionally brewed beers lacked, it is curious that there was no product claim to the 'new' beer itself.

This was a surprising omission, especially when it is understood that by 1873 America was home to some 4000 breweries; yet even more surprising was that Pasteur claimed 'pure yeast', defined as '[y]east, free from organic germs of disease', as an invention. Why

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[21] Federico, P.J. (1937), 'Louis Pasteur's Patents', *Science*, New Series, 86 (2232), 327.

[22] Which led Eduard Buchner to discover in 1897 that yeast contained an enzyme, which he called 'zymase', and it was this enzyme that caused sugars to ferment and for which he was awarded the Nobel Prize in Chemistry in 1907.

he claimed an intermediate product used in the brewing process but not the final product – the beer itself – is difficult to comprehend especially when the final product was not only completely artificial, but was also far more valuable. By contrast, pure yeast was not only a derivative of a natural substance but it performed the very same function as natural yeast, with its only distinguishing feature being its purity. While purity was important in terms of the role it played in Pasteur's brewing process, its purity neither changed nor enhanced its ability to perform its natural function. In actual fact, it was identical to natural yeast in that respect.

In 1876 Pasteur published details of his beer inventions in a book, *Études Sur La Bière, Ses Maladies, Causes Qui Les Provoquent, Procédé Pour La Rendre Inaltérable; Avec Une Théorie Nouvelle De La Fermentation*. The book was so popular with brewers that Frank Faulkner, a noted British brewer of the day, translated it into English and published it in 1879 as *Studies on Fermentation: The Diseases of Beer, Their Causes and the Means of Preventing Them*. Impressed with Pasteur's ideas, Faulkner wrote: '[t]he more I studied the work, the more I was convinced of its immense value to the brewer as affording him an intelligent knowledge of the processes and materials with which he deals.' Pasteur was also granted patents over the same inventions in France, Italy and the UK. Yet, despite the readiness with which his ideas found favour with brewers and the grant of these patents, according to Federico, 'in all likelihood no attempts to commercialize the inventions were ever made'.

One explanation might be that Pasteur was not a particularly astute businessman. Another might be that he was not particularly litigious. Yet another, as Federico hinted, was that the second of his US patents was of questionable validity. Citing *Brogdex* (decided in 1931), he opined that Pasteur's second patent: 'would now probably be refused by an examiner, since it may be doubted that the subject-matter is capable of being patented'. Of course, it may have been the case that even in 1873 the patent was considered to be invalid on the basis of the law as it stood at the time; and although *Brogdex* was decided some fifty years later, had its reasoning been applied to the Pasteur patent over 'pure yeast' in the same way as it was applied to the borax coated orange, then it would seem that the claim to purified yeast would also have been held to be invalid.

When it is understood that in 1931 patentable subject was, with the exception of one word[23], defined the same as the current US patent legislation provides (which Federico help to draft and for which his famous words are ascribed), how could it be that anyone would seriously argue that isolated or purified biological materials could be patentable subject matter? Surely, if anyone was in a position to broaden the scope of patentable subject matter in 1952, Federico was.

Yet Mathew Rimmer, an Australian intellectual property law academic, in his recent survey of the law[24] seems to adopt the same position that has been adopted by some American patent law commentators, who subscribe to the view that *Chakrabarty* '"changed the default position on protecting life-sciences materials"'.[25] Apart from calling to 'an end to the default position', Rimmer argues that patent law 'should be technology-specific, especially when dealing with the demands of particular kinds of biotechnology', and agrees with economists Adam Jaffe and Josh Learner[26] that the US patent system 'is "broken" and

[23] The 'process' in lieu of 'art'.

[24] Rimmer, Matthew (2008), *Intellectual Property and Biotechnology*, Cheltenham UK and Northhampton, US: Edward Elgar.

[25] Ibid, 299, quoting Helen Berman and Rochelle Cooper Dreyfuss (2006) 'Reflections on the science and law of structural biology, genomics, and drug development', UCLA Law Review, 53, 871-908, 873.

[26] Jaffe, Adam B. and Josh Lerner (2004), *Innovations and Its Discontents:*

to be needs reformed.'[27] Apart from the fact that the recent attempt to reform the US patent system has ground to halt[28], the fact remains that *Chakrabarty* did not give the CAFC nor the USPTO carte blanche over the patenting of biological materials. In truth it is somewhat of an oversimplification to suggest that it changed 'the default position'. That is not to say, however, that it has not been represented as such by US patent attorneys to US policymakers and legislators. Before a US House Committee,[29] Andrea Ryan, the then President-Elect of the American Intellectual Property Law Association, an association of US patent attorneys, testified that *Chakrabarty* confirmed: 'any product of nature is patentable if it is transformed *in some way* by man and it is also new, useful, and non-obvious'.[30] She expressly used the phrase 'in some way' to deliberately suggest that the US Supreme Court in *Chakrabarty* had ruled that any human intervention would be sufficient to distinguish a product of nature from a patentable biological material; yet the US Supreme Court in *Chakrabarty* had said no such thing. The Chief Justice had made it clear in his decision that what was required for a biological material to meet the threshold of invention was the display, by the modified biological material, of markedly different characteristics to anything found in nature (that is, it performed a function that was unprecedented in nature and had significant utility), and Ryan well knew that the mere isolation or purification of a biological material came nowhere near satisfying that criterion. Unfortunately, her misdescription of the Chief Justice's reasoning could not be dismissed as a mere oversight, but was a deliberate attempt to misinform, because she then persisted, by suggesting that the real issue in patent law in the light of *Chakrabarty* was no longer, 'whether an isolated or purified product obtained from nature, such as a gene-based invention, [was] eligible for patenting', but what was, 'the proper form and scope of the application and claims for the patent to be granted?' In other words, the Subcommittee was invited to accept that the US Supreme Court permitted the patenting of isolated or purified biological materials, and if there were problems that needed to be addressed in terms of the impact which the US patent system was having on medical and scientific research, then the solutions were to be found in the way the patent system was being administered.

What has been missing in this debate is a careful and considered assessment of what the Chief Justice decided, and how his reasoning could be applied beyond the specific facts of the case and the patent in issue in *Chakrabarty*.

The phrase 'anything under the sun made by man' is synonymous with the word 'new' in s.101 and while what is new and what is not seems an easy distinction to make, deciding whether something is 'made by man' or nature, is not. Fortunately, the Chief Justice was quiet specific about what kind of human intervention would transform a product of nature into a product of man, but in the resulting stampede that marked the beginning of the biotechnology gold rush, this qualification was simply ignored.

The invention described in US 3,813,316, entitled '*Microorganism*

How Our Broken Patent System is Endangering Innovation and Progress, and What to do about it, Princeton, US: Princeton University Press.

[27] Rimmer, op cit 24, 299.

[28] See *Managing Intellectual Property*, 12 May 2008, which confirmed that the Us patent reform bill 'has been stalled for some time due to a lack of agreement on key issues …'.

[29] US House of Representatives, Judiciary Subcommittee on Courts and Intellectual Property *Gene Patents and Other Genomic Inventions*, 13 July 2000.

[30] Ibid, Statement of M. Andrea Ryan, 13 July 2000.

having multiple compatible degradative energy-generating plasmids and preparations thereof', granted on 28 May 1974, was a genetically modified bacterium. Six years later, amid enormous controversy, the US Supreme Court confirmed it to be a 'new' composition of matter and, therefore, patentable subject matter. Although it was derived from nature, the Court found that, unlike the natural bacterium, it contained 'two stable energy-generating plasmids, each of which provided a separate hydrocarbon degradative pathway', which the natural bacterium did not. Dr Chakrabarty's insertion of these two plasmids, through the use of what was then a leading edge molecular biological technique, was held by the Chief Justice to have transformed a natural bacterium into something that was 'made by man' because: 'the patentee has produced a *new* bacterium with *markedly different characteristics from any found in nature* and one having the potential for significant utility.' By a narrow majority of 5 to 4 the Court ruled that Chakrabarty's discovery was: 'not nature's handiwork, but his own; accordingly it [was] patentable subject matter under ß 101.'

Undoubtedly, it was artificial in some degree. Undoubtedly, it was derived from nature. Undoubtedly, it had a commercial and industrial application and, undoubtedly, it was valuable. However what actually convinced the Court that it was a new 'composition of matter' was that it displayed 'markedly different characteristics from any found in nature'. Indeed the biological function that it performed had no natural precedence. For the first time ever, an organism was capable of degrading crude oil. The Chief Justice emphasised that this was a significant degree of artificiality – one that so changed the organism that it could no longer be said to be a product of nature. The Chief Justice considered three characteristics about Chakrabarty's bacterium to be crucial: the level of human intervention, the end result (its function) that was unprecedented in nature and the significant utility that this function had.

In the first instance, the artificial bacterium in *Chakrabarty* was *significantly modified* when compared to any natural microorganism, not just the bacterium in issue. The human intervention involved the genetic modification of a natural bacterium through the insertion of two plasmids that were not found in any naturally occurring microorganism.

In the second instance, the microorganism displayed *markedly different characteristics from any found in nature;* namely it degraded crude oil. There was no naturally occurring microorganism or anything close to it that performed this function. The Court's emphasis here was not on the artificial bacterium performing a new function in comparison to the natural bacterium, but on the artificial bacterium performing a function different from *any* found in nature. It did more than simply *replicate or reproduce* an identical substance or thing already produced in nature, such as insulin, human growth factor, hepatitis C virus, erythropoietin, human tissue plasminogen activator or Factor VIII: C.

Finally, the microorganism's ability to degrading of crude oil had the *potential for significant utility* that was directly attributable to its new characteristics – characteristics that were alien to nature.

Only in satisfying all three criteria did the US Supreme Court rule that Chakrabarty's bacterium was something that was an 'invention', or patentable *subject matter*. Of course to be a patentable invention Chakrabarty's invention had to also satisfy the secondary conditions of patentability: namely novelty, obviousness and written description. Thus the US Supreme Court emphasised that it was the *new* characteristics per se which possessed the potential for *significant* utility, not simply the *artificiality* of the bacterium per se that proved decisive. What was crucial in this process of transformation was the degree of human intervention, which was significant, and how

that directly contributed to its *new* function of degrading crude oil. The microorganism was not merely 'isolated' from its natural environment, nor purified through a process of manufacture.

Indeed, there was nothing revolutionary about the Chief Justice's reasoning and it was consistent with previous US Supreme Court authority, including *Brogdex* and an even earlier case, *Cochrane & Others v Badische Anilin & Soda Fabrik* (1884) 111 US 293 (*BASF*) in which the US Supreme Court held that 'artificial alizarin', a chemical dye that was identical to alizarin, a natural dye made from the Madder plant, was not patentable subject matter. In fact, according to the Court, that it was made through an artificial process was irrelevant to defining what it was. There Justice Blatchford held: '[c]alling it artificial alizarin did not make it a new composition of matter, and patentable as such, by reason of its having been prepared artificially for the first time from anthracine, if it was set forth as alizarin, a well known substance.'

Thus *BASF*, *Brogdex* and *Chakrabarty* are US Supreme Court authority to the effect that under present US patent law, biological materials that are derived from nature and that are essentially indistinguishable from those materials, even if isolated and purified, are not patentable subject matter. What has been lacking so far is the proper application of the law which, unfortunately, in the hands of the CAFC, which has been off on a frolic of its own, has been misapplied, misunderstood and mostly absent.

It would seem that what is needed is for the law to be reasserted as it has been written and interpreted by the US Supreme Court. Clearly, if *Laboratory Corporation of America Holdings v Metabolite Laboratories, Inc* (2006) 548 US is any indication, then it is possible that once again the detour made by the CAFC will be closed. Even though the Court subsequently withdrew *certiorari*, Justices Breyer, Stevens and Souter, in their powerful dissent, made it clear that patentable subject matter was an important threshold that should not be transgressed. They were critical of a patent that sought to control the diagnosis of a vitamin deficiency, based upon the measure of a naturally occurring amino acid, homocysteine, in the human body. Unfortunately, LabCorp had failed to raise the issue of patentable subject matter before the lower federal courts and only raised the issue before the US Supreme Court in their application for *certiorari*. This meant that there was an absence of evidence upon which the appeal Court could properly assess the issue; at least this was the view of the US Attorney-General and the majority of the Supreme Court. In referring to the principal of US patent law which, 'excludes from patent protection … laws of nature, natural phenomena and abstract ideas', Breyer confirmed, 'this principle finds its roots in both English and American law', and he explained that its existence, 'does not lie in any claim that "laws of nature" are obvious, or that their discovery is easy, or that they are not useful'. '[T]o the contrary', he held, 'research into such matters may be costly and time consuming; monetary incentives may matter; and the fruits of those incentives and that research may prove of great benefit to the human race'; but even so, 'the reason for the exclusion is that sometimes too much patent protection can impede rather than "promote the Progress of Science and useful Arts"'.

The idea that literally 'anything under the sun made by man' is patentable subject matter misrepresents the law. The Chief Justice's words, just as the words of P.J. Federico from whom they were borrowed, have been deliberately stretched and distorted to the point that they have lost any sensible meaning, yet when one understands them in the context in which they were spoken, then it is apparent they do not support the 'broad holding' of the Constitutional power.

One hundred years after Pasteur was granted a US patent over an improved beer making process, which included a claim to purified yeast, Cohen and Boyer discovered that it was possible to cut DNA

from the genome of one organism and splice it into the genome of another. Their discovery, like Pasteur's discovery of 'pernicious germs', was so revolutionary that it forever changed scientific thinking, contributing to a body of knowledge that finally enabled scientists to adapt nature's processes to manufacture biological materials in vast quantities and with a purity that was hitherto thought impossible. They were acknowledged as inventors on a US patent, although it was their university, not them, that received millions of dollars in royalties; but Stanford never exercised its patent rights to exclude others from using the 'invention' made possible by their discovery. Rather, the university's policy of non-exclusive licensing enabled Genentech, a company that Boyer co-founded, to patent the genetic material of the human gene that encoded human insulin, a natural substance that was made using genetic material that no one invented. Unchallenged, the patent proceeded to make both Boyer and Genentech rich and their success sparked a new rush – not for gold but for genes.

Cohen and Boyer's discovery of how to use the cellular components of natural cells to express a protein encoded by foreign DNA was a scientific breakthrough; but imagine a situation in which cells have been constructed in a laboratory using amino acids. Imagine again that these cells have been engineered so that they contain genetic material that encode for a human protein; and, further, that these cells have expressed that protein. Both the cell and the protein are artificial – both are synthetic.

According to Jonathan Tucker and Raymond Zilinskas[31] '[t]he main difference between genetic engineering and synthetic biology is that whereas the former involves the transfer of individual genes from one species to another, the latter envisions the assembly of novel microbial genomes from a set of standardized genetic parts.' These standardized genetic parts are themselves products that enable the construction of a synthetic genome, much like other types of manufactured components enable the construction of machines. The implication here is that, like machines, the synthetic genome, being the sum total of these genetic parts, is patentable subject matter and that to the extent that these, 'natural genes … have been redesigned to function more efficiently or … have been designed and synthesized from scratch', they meet the subsidiary thresholds of novelty and inventive step. Their analysis, therefore, suggests that these synthetic genomes are patentable inventions. Indeed, the efficiency of synthetic genomes over genetically modified 'natural genes' to express proteins is supposedly an improvement that is useful, in that it purports to improve cellular productivity, which in turn makes them valuable. Accordingly, they *appear* to possess the attributes of things that have traditionally met the requirements of invention; but do they qualify?

On 25 January 2008 *The Independent*, a London newspaper, published an article written by Steve Connor, the science editor, carrying the headline: 'Playing God: the man who would create artificial life'. It was about Craig Venter, 'the controversial American scientific entrepreneur', who was described as such, no doubt, because his company, Celera Genomics, had managed not only to map the entire human genome, but had sought to patent it. The attempt raised such serious issues and public outrage at the time that it led US President Clinton and UK Prime Minister Blair to issue a joint statement in March 2000 condemning it and making it clear that the human genome belonged to no man; it was a resource that should be freely available to all researchers.

Publicly rebuked and eventually removed by the Board as Celera's CEO, an undaunted Venter eventually turned his attention towards

[31] Tucker, J.B. and Zilinskas, R.A. (2006), 'The Promise and Perils of Synthetic Biology', *The New Atlantis*, 25–45.

Mycoplasma gentialium, a parasitic microbe that lives in the reproductive tract. Using the conventional cloning methods pioneered by Cohen and Boyer he developed a process into which sections of the genome of Mycoplasma gentialium were housed in 'cassettes' that when assembled in a laboratory, produced the completed 'synthetic' genome. The sensational headline, no doubt designed to attract the public's attention, proclaimed that Venter's synthetic version of Mycoplasma gentialium meant that he had created 'artificial life'; yet this was mere conjecture and until such time as the synthetic genome is actually 'booted up', it will remain so. Yet Venter plans to try and if he is successful he and his colleagues will probably claim to have created a synthetic life form made using synthetic biology. Their hypothesis is that these synthetic organisms will then replicate like natural organisms and, applying the protein synthesis idea first conceived of by Cohen & Boyer, they expect that they will synthesise proteins. Naturally, this potential means, like natural and genetically modified organisms, that these synthetic organisms have the potential to become new 'unnatural' pathogens. Unperturbed, Venter has allegedly modified the synthetic genome of Mycoplasma gentialium so that it contains, according to Connor, 'self-destruct mechanisms' that make it impossible to, 'survive beyond the confines of a laboratory.' This, of course, implies that Venter knows all that there is to know about how Mycoplasma gentialium will behave once the synthetic version is 'alive', and can guarantee that it will not mutate around this safeguard, but can he? Moreover, the question remains: what have he and his co-inventors invented?

On 15 November 2007 the patent application US 20070264688, modesty entitled 'Synthetic Genomes', was filed by Venter and his co-inventors. The principal invention was defined as: '[a] method for constructing a synthetic genome comprising: assembling nucleic acid cassettes that comprise portions of the synthetic genome, wherein at least one of the nucleic acid cassettes is constructed from nucleic acid components that have been chemically synthesized, or from copies of chemically synthesized nucleic acid components'. That is merely the beginning - the patent application makes it clear that the inventors contemplate that their method will be applied to construct all manner of genomes, including a 'eukaryotic cellular organelle'; 'a bacterial genome'; 'a minimal genome'; 'a minimal replicating genome'; anything that 'is substantially identical to a naturally occurring genome'; 'a non-naturally occurring genome'; 'a synthetic cellular genome' and '[a] synthetic genome'. The patent application also contains claims to cellular components, such as: 'nucleic acid[s] … that have been chemically synthesized or [made] from copies of the chemically synthesized nucleic acid components' and 'sequences that allow production of a product of interest'. Finally, there are claims to products such as 'an energy source' (undefined in the patent specification other than by reference to 'hydrogen or ethanol'), and, 'therapeutics and industrial polymers'.

The subject of this invention is: 'a synthetic version of the Mycoplasma genitalium genome having 482 protein-coding genes and 43 RNA genes comprising a 580-kilobase circular chromosome'. In fact, the natural bacterium has one of the smallest genomes of any known bacterium; clearly the reason why Venter chose it to test his hypothesis. Accepting that the 'invention' is the method, one of its glaring deficiencies is its attempt to capture within the scope of the proposed patent monopoly *any* method of 'constructing a synthetic genome' using nucleic acid cassettes. Thus, the product-by-process claims also seek patent monopolies over things, such as a 'eukaryotic cellular organelle', constructed synthetically using any method employing nucleic acid cassettes.

The first problem with this approach, as previously discussed, is that the US Supreme Court ruled in *BASF* that this type of patenting is unacceptable. In this case, the patent seeks to cover the technological field of making a synthetic genome, howsoever this is

performed. Even though it refers to 'cassettes', suggesting that the assembly will be completed using more than one cassette, it does not exclude the possibility that the synthetic genome can be assembled into one giant cassette. All that the patent application actually requires is for 'at least one of the nucleic acid cassettes' to be constructed from nucleic acid components that have been 'chemically synthesized'. This means that if the entire genome can be chemically synthesized (that is, made using conventional techniques) in a single operation then, the genome being in a 'nucleic acid cassette', any method that achieves this will come within the scope of the claim. Obviously Venter and his colleagues are not content to patent a specific method; their intention is to obtain a patent monopoly over all biological materials that are synthetically constructed and the product-by-process claims will, theoretically, achieve this if the method claim is so understood. In this respect, the patent monopoly of claim 32, which is to the 'synthetic genome' per se as a product, will automatically capture all methods of making it. Other claims tend to corroborate this conclusion; for instance claim 38, which is to: '[a] method comprising: designing a synthetic genome; constructing the synthetic genome; introducing the synthetic genome into a biological system; and expressing the synthetic genome.'

The second problem is that neither Venter, nor anyone else, designed or created the genome of Mycoplasma genitalium. Apart from being made in a laboratory, the truth is that the synthetic version of this natural bacterium is substantially identical to the natural. Perhaps, as Venter purports to have done, the genome has been tweaked so that it cannot infect humans, but it is so closely related to the natural bacterium that it would be a misrepresentation to suggest that it is sufficiently different to the natural that it satisfies the thresholds established by the US Supreme Court in either *Brogdex* or *Chakrabarty*. The fact that it is incapable of infecting humans is not the kind of difference that would distinguish it either in 'form, quality or property' (*Brogdex*) nor the kind of functionality that would be 'markedly different characteristics to any found in nature' (*Chakrabarty*). Consequently, the patent specification merely provides particulars of a method that produces something that, frankly, is not patentable subject matter. That it is synthetic does not make it an invention (*BASF*).

The third problem is that, while the synthetic bacterium may provide the technical platform for the production of a synthetic 'energy source', the claims do not seek a patent monopoly over a form of synthetic hydrogen or ethanol that is any way different to hydrogen or ethanol produced naturally or by any other methods (*BASF*). In point of fact, nowhere in the patent application is there any information about how to make the synthetic 'energy source' made using the inventors' methods. Apart from describing a single method of constructing the bacterium, the patent specification appears to be completely devoid of anything that is inventive.

A week later, on 22 November 2007, Venter and his co-inventors filed US 20070269862 - a patent application entitled *Installation of genomes or partial genomes into cells or cell-like systems*. The invention, acknowledged to have been 'made with government support', is defined as: '[a] method for making a synthetic cell, the method comprising: obtaining a genome that is not within a cell; and introducing the genome into a cell or cell-like system'. Also claimed as an invention is: '[a] synthetic cell produced by obtaining a genome that is not within a cell, and introducing the genome into a cell or cell-like system'. There was no claim to 'synthetic human insulin', but the patent specification states that 'insulin peptides' could be 'collected' from 'synthetic cells'; clearly signaling that the inventors are contemplating that human insulin is one of the proteins that may be made using the invention.

If this patent application is granted in this form it would seem likely that the world will face the prospect of a new round of

patents over the production of human insulin, erythropoietin and the myriad other proteins that are pharmaceutically useful. In the case of insulin, should this occur, it will mean that since 1922 three different patent monopolies have controlled its production. The first, for purified insulin extracted from animal pancreases, was between 1922 and 1939; the second, for purified human insulin made using recombinant DNA, was between 1978 and 1995; and a third, for synthetic human insulin made using synthetic cells, although not yet a reality, is still a foreseeable possibility.

That being said some synthetic biologists are also proposing to modify nature's blueprints. The question is: will these modifications change the protein which the gene encodes or will they merely improve the production of natural proteins? This is an important distinction, because even if these genes are substantially different from natural genes and are enhanced, if the proteins which these synthetic cells express are identical to, or are substantially identical to, natural proteins then the proteins themselves are not *new*. The idea that 'anything under the sun made by man' is patentable subject matter suggests that artificiality is the key to invention, but there is, as has been argued here, much more to invention than that. Even putting to one side the patentability criteria of novelty, inventive step and industrial applicability and focusing only on the issue of patentable subject matter, it is undoubtedly the case that artificiality, while being one of the necessary criteria of invention, is by no means the only criterion. The essence of invention is not mimicry but something 'new', and not in the sense of being novel but in the sense of being an 'invention' (*BASF*; *Brogdex*; *Chakbrabarty*). To merely replicate nature's protein products using natural genetic material, even if that material is synthetic and enhanced, is not making something 'new', because the protein will be the same as the natural protein (*BASF*). Therefore, while these synthetic cells are artificial and they incorporate into their genetic structure DNA that has been genetically modified from its natural equivalent, do the products that they produce 'display markedly different characteristics not found in nature'? Unless they do, these products are not patentable subject matter. Furthermore, to the extent that the processes employ synthetic genes that are substantially identical to natural genes, the processes will also not be patentable because they too are not *new*, or are *obvious*.

Even so, there is still a long way to go. Despite all the hyperbole, much of what synthetic biologists have achieved so far is to augment natural proteins with some unnatural amino acids; and as fascinating as their research is, they have yet to produce anything that comes close to being a complete new protein that truly is an invention. For example, Thomas Magliery from the Department of Molecular Biophysics & Biochemistry at Yale University writes[32] that synthetic biology has enabled the 'reprogramming of the templated synthesis of proteins'. While the paper describes how an 'unnatural amino acid' has been incorporated into the genetic structure of a natural bacterium so that it 'does not require minimal medium for culturing [and] may be suitable for more ambitious organismal engineering projects', it still remains something that is substantially identical to the natural bacterium from which the vast majority of its amino acids are derived.

Nonetheless, Magliary warns that this new science comes with 'the caveat that containment of the bacterium is exceedingly important'. Just as in the mid-1970s, when the NIH moved to regulate experiments that used genetically modified microorganisms,[33] caution needs to be

[32] Magliery, T.J. (2005), 'Unnatural protein Engineering: Producing proteins with Unnatural Amino Acids', *Medical Chemistry Reviews-Online*, 2, 303-323.

[33] Paul Berg, David Baltimore, Hebert Boyer, Stanley Cohen, Ronald Davis, David Hogness, Daniel Nathans, Richard Roblin, James Watson, Sherman

exercised with synthetic biology. Perhaps even more so, for now scientists are not merely tinkering with the genomes of natural biological materials but are attempting to create biological materials that are potentially alien to nature. The consequences of such engineering must be fully understood; and it is clear that at the present time they are not.

Despite this risk, progress in synthetic biology continues. As Jianming Xie and Peter Schultz, who is one of America's leading synthetic biologists, have explained, 'although a 20-amino-acid code might be sufficient for life, it might not be optimal'.[34] By this they mean that the use of non-natural amino acids may lead to the manufacture of therapeutically useful proteins that are significantly different to natural proteins and that perform *in vivo* in significantly different ways. They envisage, for example, the possibility of being able to produce proteins that exhibit an efficacy that is superior to natural proteins or that may provide new ways for protein drug delivery. They explain that at this stage in the science: 'over 30 unnatural amino acids have been co-translationally incorporated into proteins with high fidelity using a unique codon and corresponding transfer-RNA;aminoacyl-tRNA-synthetase pair.'

Of course, the synthesis of proteins still relies on natural microorganisms, such as yeast and E. coli. This is confirmed by Wenshe Liu[35], who has described experiments where protein synthesis is undertaken with the use of cells derived from Chinese hamsters, a mammalian cell line. He and his co-authors conclude that their method represents a further advance in synthetic biology because: '[it] should facilitate cellular studies using biological probes [and ultimately] may allow the synthesis of therapeutic proteins containing unnatural amino acids in mammalian systems.'

Ambrx, the company co-founded by Schultz, has already applied for patents over human growth hormones (proteins that are produced naturally in humans), using this technology. In US 20050170404, entitled *Modified Human Growth Hormone Polypeptides And Their Uses* and filed on 28 January 2005, the inventors Ho Sung Cho, Thomas Daniel, Richard DiMarchi, Troy Wilson, Bee-Cheng Sim and David Litzinger describe how they have modified natural human growth hormones so that their genetic architecture includes at least one unnatural amino acid. Their invention is: '[a] hGH polypeptide comprising one or more non-naturally encoded amino acids' derived from the 'growth hormone (GH) supergene family'. It is defined to include: 'growth hormone, prolactin, placental lactogen, erythropoietin, thrombopoietin, interleukin-2 to 13 and 15, oncostatin M, ciliary neurotrophic factor, leukemia inhibitory factor, alpha interferon, beta interferon, gamma interferon, omega interferon, tau interferon, epsilon interferon, granulocyte-colony stimulating factor, granulocyte-macrophage colony stimulating factor, macrophage colony stimulating factor and cardiotrophin-1'. Clearly, the inventors suggest that the addition of unnatural amino acids enhance hGH polypeptides, but even so they are substantially the same and they will perform essentially the same function.

Their technology potentially applies to a number of human proteins that are already being therapeutically administered as drugs, such as

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Weissman and Norton Zinder, America's most distinguished molecular biologists of the day, had signed a letter entitled 'Potential Biohazards of Recombinant DNA Molecules': *Science* ,185, 303 (26 July 1974).

[34] Xie, J. and Schultz, P, (2006), 'A chemical toolkit for proteins – an expanded genetics code', *Molecular Cell Biology*, 7, 778-782.

[35] Liu, W., Brock, A., Chen, S., Chen, S. and Schultz, P, (2007), 'Genetic incorporation of unnatural amino acids into proteins in mammalian cells', *Nature Methods*, 4 (3), 239-244

human erythropoietin which will remain subject to patent protection in the US until 2012. Amgen is the world's largest producer of human erythropoietin (epoetin alfa), sold under the trade mark Epogen, and since September 2001 has been licensed by the FDA to manufacture and supply a modified form of erythropoietin (darbepoetin alfa). This new form of erythropoietin, sold under the trade mark Aranesp, is also subject to US and international patents, but is distinct to Epogen as its therapeutic value is enhanced owing to its longer half-life, which means that its effects (to stimulate red blood cell production) last longer *in vivo* and patient dosage regimes are therefore lower. This is perhaps the kind of functional advantage[36] over human erythropoietin that satisfies the thresholds set by *Chakrabarty,* but the modification to its amino acid structure does not appear to be significant, as it comprises only of the addition of two N-glycosylation sites bringing the total number to five (whereas human erythropoietin has three). In fact, Aranesp could hardly be described as a protein that is so functionally different in 'form, quality or property' (*Brogdex*) that it could be considered to be an unnatural protein. The problem, however, is that Ambrx seeks to patent anything and everything that is made with the use of this technology, harkening back to the 1870s when BASF attempted to do the very same in the context of processes for the manufacture of artificial alizarin; an attempt that the US Supreme Court ruled to be illegal (*BASF*).

Beyond the sheer breadth of the scope of such patent claims in terms of their potential use, other issues arise because of the terminology used to define the unnatural proteins. For instance, in the International Preliminary Report of Patentability, published in accordance with the Patent Cooperation Treaty (PCT) on 24 May 2007, an objection to patentability of Ambrx's patent was raised merely because the term 'non-naturally encoded amino acid' was 'unclear and could mean either an artificial amino acid or a naturally occurring amino acid substitution'. The report also questioned the novelty of the invention, citing an earlier US patent, namely US 6,608,183[37], on the basis that it disclosed information about a human growth hormone that had also been genetically modified by a natural amino acid substitution. The effect of this substitution was to increase the 'stability and half-life' of this hormone and, consequently, it cancelled out the only significant distinguishing feature in terms of its patentability.

So far these remain patent applications and only time will tell whether they make it through the USPTO, but even if they do, history confirms that they may not be valid patents. Still, given the multitude of patents that are granted every day and how many go untested in the courts the likelihood is that they will make it through and in doing so will perpetuate the myth that literally anything is patentable. Whether they survive, however, will depend on a number of factors, namely whether those that are affected have the *locus standi*, will power and very deep pockets needed to mount a challenge through the US court system all the way to the US Supreme Court.

[36] Although the FDA has issued warnings over its use for cancer patients.

[37] US 6,608,183 (19 August 2003), *Derivatives of growth hormone and related proteins*.