The Patenting of Biological Materials: A brief history of a concerted attempt to bring this practice to an end in Australia.

Luigi Palombi

Introduction

In 2008 four Australian patents granted to Myriad Genetics were used by Genetic Technologies, a Melbourne company that had patented junk DNA and was also Myriad's exclusive licensee, to try and do in Australia what Myriad had done in the United States - to monopolize the genetic testing for the human BRCA gene mutations linked to breast and ovarian cancers.

With the patent 'rights' to these gene mutations, found on human genes BRCA 1 (located on human chromosome 17q) and BRCA 2 (located on human chromosome 13), Genetic Technologies could legally exclude anyone from making, using, selling or dealing with these gene mutations for any purpose for 20 years.

On July 7 the company sent a letter to every Australian laboratory known to be providing BRCA gene testing to Australian patients. The letter, signed by its president, Michael B Obanessian, gave each of them 7 days to cease "using the Patents" and "refer the performance of all BRCA 1 and BRCA 2 testing" to the company or be sued for patent infringement. Mr Obanessian stressed the urgency of the threat: "Our lawyers have prepared a detailed Statement of Claim and are ready to file an Application with the Federal Court if necessary."

I am very pleased to advise that it never became necessary.

What Mr Obanessian and Genetic Technologies hadn't realized was that this letter, far from being a "warning shot fired across the bow", as one patent attorney was to later describe it to a Senate Committee charged with investigating the impact of gene patents on the Australian healthcare system, lit a fuse - a fuse which is slowly sizzling towards its ultimate goal - the obliteration of patents over naturally occurring biological materials in Australia.

National media coverage broke the story with headlines such as "Patent bid sparks fear of price hike for cancer test" and "A price on your genes", galvanizing Australians into action.

My reaction was to immediately contact the president of Cancer Council Australia, Prof Ian Olver, volunteering my services. I pleaded with the CCA to bring a test case to challenge the validity of the patents in an Australian court. I made it clear it would all be pro bono. The media picked up on this offer with "Lawyer looks at breast gene patent", but the CCA decided not to sue. It couldn't afford to run the risk of losing a case which, in Australia, would have translated into it having to pay not only Genetic Technologies's legal costs, but also Myriad's. The potential multi-million dollar liability was too great for CCA to bear.

So I went to see Senator Bill Heffernan, one of Australia's most well known politicians. I'd met the senator some years before when I was one of a small army of post-docs that had descended on the Parliament to meet two politicians, their names pulled out of hat, to tell them about their research interests. It was almost like a school excursion except I was 47 not 14. Little did I realize then that the genuine interest which the senator showed in my PhD research would be the

precursor to a full scale Senate inquiry. On November 12, 2008 the senator rose to his feet in the Senate Chamber to "thank the Senate for its generosity in agreeing to an inquiry into the impact of gene patents on the provision of health care in Australia." And so began a process which has led to the *Patent Amendment (Human Genes and Biological Materials) Bill, 2010.*

The Senate Community Affairs References Committee's Inquiry into Gene Patents

It had been a long, detailed and complex inquiry with 77 submissions and many private and public hearings. Membership of the committee had also changed with some senators being replaced at the start of a new parliamentary year in 2010. The general election, a new Prime Minister and the inevitable delays which flowed on during 2010 pushed out the report date yet again. The opening hearing was held on March 19, 2009. It was meant to be over by the November but that date came and went. Finally, on November 26, 2010 the Committee released its long awaited report.

The report, however, was disappointing in one sense - it contained no recommendation for a specific amendment to the *Patents Act, 1990* to expressly ban patents on naturally occurring (isolated) biological materials. In another, it was a revelation, dovetailing with the March 2010 decision of Judge Sweet in *Association for Molecular Pathology et al v United States Patent and Trademark Office et al*, by "strongly" rejecting the argument made by the Australian patent office, IP Australia, that "genetic information that is isolated from its naturally occurring state in the human body may be classed as an invention".

The tension within the Committee over this issue had been palpable. IP Australia was adamant, intransigent and unrelenting. According to the Commissioner of Patents, Ms Fatima Beattie, it had been the accepted position for more than 100 years that isolation was a legitimate step in arriving at a chemical invention. I have no doubt, having witnessed her testimony time and again, that the Committee members struggled throughout the course of its Inquiry to come to terms with the competing claims. On the one hand was the Commissioner of Patents, Ausbiotech (Australia's equivalent of the U.S. Biotechnology Industry Organization), the Institute of Patent and Trade Mark Attorneys of Australia (IPTA), and The Law Council of Australia (to name a few). On the other side were some scientists, Cancer Council Australia, a few patient advocacy groups, a handful of concerned citizens, some of my colleagues at the Australian National University and me. And despite what was to my mind blatantly obvious, that something that occurred in nature, even when removed from its natural environment, was a natural phenomenon, it was not until the filing of the United States Department of Justice amicus brief, filed on October 29, in the Myriad appeal that the Committee was capable of standing up to the Commissioner.

Those who urged the Committee to accept IP Australia's position were well organized, well funded and had an army of lobbyists at their disposal. IPTA relentlessly attacked my credibility portraying me as an idealist - the quixotic zealot - befuddled by my own lack of understanding of commercial reality. They argued that without patents the research money for developing new and inventive diagnostics, drugs and therapies would dry up. Publicly funded research, they said, "would not lead to private profit" and this was essential if the "hugh expense in making these products available to the public [was] not linked to the patent

system." The usual specious arguments, which had already been put forward in the United States in response to the ACLU's initiative, were repeated here: "without the existence of a patent monopoly, no company will take the risk of investing millions of dollars to bring a product to market".

Necessity is the Mother of Invention, Not Patents.

Of course they are specious. What the defenders of the status quo conveniently overlook is the role played by scientists at universities and research institutes who, but for the public funding provided to them and their institutions through various government grants, would never be able to make the breakthrough discoveries that private research funders would never have been able to undertake in the first place. They forget that the greatest scientific breakthrough of the 20th century, penicillin, the world's first antibiotic, was developed in a publicly funded university in England by a team of scientists led by the famous Australian, Prof Howard Florey. They forget that it was Prof Mary-Clare King who, with the aid of public funding, labored for 16 years at UCSF to produce sufficient data to link a gene on human chromosome 17q to breast and ovarian cancer in women. They forget that it was Dr Daniel Bradley at the Centers for Disease Control who developed the chimpanzee plasma pool without which Chiron would have had no chance of cloning the hepatitis C virus. They forget about the important role Dr Eugene Goldwasser, from the University of Chicago, played in the cloning of erythropoietin, a human protein, administered to renal and chemotherapy patients in a synthetic form as a biopharmaceutical to help them overcome anemia. And yet information about the role these and many other scientists in publicly funded research institutes have played in bringing modern diagnostics, medicines and therapies to humanity are repeatedly ignored by those who are determined to convince policymakers and politicians that the sole source of funding for these kinds of developments is private. Even worse, that without patents, even that funding would dry up. In December 2010 the Chicago Tribune published an obituary of Dr Goldwasser. This is what it said:

> Dr. Eugene Goldwasser, 88, a University of Chicago biochemist who identified one of the body's key hormones and helped launch a new drug that revolutionized dialysis treatment, died Friday, Dec. 17, in his Hyde Park home of complications due to prostate cancer, said his family.
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> In 1977, after nearly 25 years of research, Dr. Goldwasser discovered the hormone secreted by the kidneys known as erythropoietin or EPO, which controls production of oxygen-carrying red blood cells.
>
> He shared his discovery with a California-based biotechnology firm, Amgen Corp., which developed an artificial version of the hormone. In 1989, Amgen won federal approval for the first EPO drug to treat anemia in dialysis and cancer patients. In later years, other drug companies manufactured their own brands of EPO, spawning a billion-dollar industry.[1]

I think this brief history of one scientist says all that needs to be said. And the time has come for the truth to be screamed from the rooftops - it is not patents

[1] Margaret Ramirez, *Dr Eugine Goldwasser, 1922-2010, Biochemist behind lifesaving drug father of EPO*, Chicago Tribune, December 21, 2010.

that drive invention, it is necessity. And also to clarify, Dr Goldwasser was not, despite the headline, the father of erythropoietin. He did not invent it.

Lies, lies. All lies.

Do we ever ask: what drove invention before the development of letters patent? A letter patent was a device first used by monarchs in the 13th century to create monopolies over anything. The rich Venetian State took this idea further in the 15th century and developed the world's first patent system to reward the act of invention with a time-limited monopoly. And while there is merit in the idea that those who share the practical and useful fruits of their genius or ingenuity with society should be given a way of recouping their investment in time and money, an idea borrowed from the French revolution and enshrined in the U.S. Constitution, it is going too far - way too far - to extend that privilege to all and any form of innovation. Doing so is dangerous because it may encourage the reemergence of the kinds of monopolistic behavior outlawed in 17th century England. Even so it is a lie to suggest that without patents there will be no innovation or invention. And those that perpetuate this lie are putting their own self interest above the interests of humanity. More than that, they use that lie to perpetuate another (that natural biological materials once isolated from their natural environments are the product of invention) to suggest that without patents research and development of gene based inventions will not happen. This is a gross exaggeration. The U.S. Department of Justice has admitted so much in its amicus brief filed in the Myriad BRCA patent appeal. Having first acknowledged that its brief ran counter to a "longstanding practice of the Patent and Trademark Office, as well as the practice of the National Institutes of Health and other government agencies", the DoJ made this concession:

> The chemical structure of native human genes is a product of nature, and it is no less a product of nature when that structure is "isolated" from its natural environment that are cotton fibers that have been separated from cotton seeds or coal that has been extracted from the earth.

Yet, in spite of the U.S. government's about face the Australian Commissioner of Patents is maintaining the lie. On March 22 she told the Australian Senate's Legal and Constitutional Affairs Legislation Committee, which is currently investigating the *Patent Amendment (Human Genes and Biological Materials) Bill*, that "substances isolated from nature for which a practical/industrial use has been identified have been consider INVENTIONS since the inception of the Australian patent law". In other words, if someone discovers a tree (let's assume for the first time), chops it down, removes its branches and leaves, strips its bark and mills it into planks of wood, they invented the tree. This is just plain nonsense.

In Europe, however, the lie has been turned into law. In 1998 the European Parliament passed the European Biotechnology Directive. As a result all EU countries transformed that lie into patent law. Article 3.2 of the Directive provides:

> Biological material which is isolated from its natural environment or produced by means of a technical process … even if it previously occurred in nature … [is patentable subject matter].

And the European parliamentarians who voted the Directive into law did so unaware that ten years earlier the United Kingdom's Court of Appeal held a European patent granted to Genentech over a human protein (human tissue plasminogen activator (t-PA)) invalid, partially because the protein itself was not an 'invention' under section 1(1) of the *Patents Act, 1977* (a provision consistent with article 52.1 of the *European Patent Convention, 1973*). Lord Justice Mustill said this:

> We are here concerned with a process for synthesising a substance identical to that which occurs in nature. The t-PA produced by the process is not 'artificial' t-PA or 'synthetic' t-PA, in the sense of artificial silk or synthetic rubber: ie in the sense of something which resembles the natural substance, or can perform a similar function, or act as a substitute. It is not ersatz. The t-PA which Genentech made is neither more nor less than t-PA.[2]

How is it possible that Europe's parliamentarians were unaware of this?

That is a question which remains unanswered in Europe. In 2004 the Danish Council of Ethics was given a mandate by the Danish government to investigate the Directive in the context of the patenting of human genes. The top level committee concluded this:

> 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.[3]

What are the consequences if the liars aren't stopped?

For an answer to this question we must go back to March 14, 2000. It was on that day that U.S. President Bill Clinton and British Prime Minister Tony Blair made a joint announcement to celebrate the decoding of the human genome; a project involving international scientific collaboration and billions of publicly funded research. In their announcement they said this:

> To realize the full promise of this research, raw fundamental data on the human genome, including the human DNA sequence and its variations, should be made freely available to scientists everywhere. Unencumbered access to this information will promote discoveries that will reduce the burden of disease, improve health around the world, and enhance the quality of life for all humankind.[4]

In other words, if we did not stop the patenting of the human genome, a process actively being pursued by many companies including Celera, headed by Dr Craig

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[2] *Genentech Inc's Patent* [1989] RPC 147 per Mustill LJ, p 262 lines 1-6.

[3] Danish Council of Ethics Report, *Patenting Human Genes and Stem Cells*, 2004, p 98.

[4] Joint Statement by President Bill Clinton and Prime Minister Tony Blair of the U.K., The White House, March 14, 2000.

Venter,[5] there was a real possibility that humanity would suffer. Their message was that the development of health-related products was not dependent on the patent system alone. Rather, that it was dependent upon the ability of scientists around the world having free and unfettered access to human genes and the products of those genes, human proteins. And while they acknowledged the role the patent system would play in "stimulating the development of important health care products" they clearly were drawing a line between products or nature, which should be freely available to all, and products of invention, which could be the subject of "[i]ntellectual property protection".

The concerns of these two important world leaders was echoed by the U.S. Supreme Court six years later. In a dissenting decision Justices Breyer, Souter and Stephens emphasized the need for a balance between what is patentable subject matter and what is not. If that balance is not properly maintained, patents, they said: "can discourage research by impeding the free exchange of information".[6]

It has been a long established and accepted principle of U.S. patent law that phenomena of nature are not patentable subject matter. But the ease with which the legal semantics, or what I have dubbed 'the isolation contrivance', have been used by patent bureaucrats, patent attorneys and their clients in a deliberate and systematic way to effectively blur the legal boundaries and game the patent system, much like tax evaders game the tax system, indicates the need for a new regulatory regime for worldwide patent governance.

This regulatory breakdown has fueled the extravagance, almost brash boldness, of the intellectual property community so much so that their clients have succeeding in turning intellectual property laws and systems into key trade related negotiation chips. In almost every bilateral and plurilateral free trade agreement which has been negotiated with the United States since NAFTA[7], intellectual property-related clauses have been inserted to extract concessions from countries keen to access U.S. agricultural markets.[8]

As a result, other forms of intellectual property have been created to aid and assist in the constriction of the public domain. Data provided to food or medicinal

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[5] Dr Venter left Celera in 2001 and is now actively trying to patent 'synthetic' microorganisms in an attempt to control the engine of synthetic hydrocarbon production and the synthetic hydrocarbons these processes produce. However, the microorganisms which Venter has sought to patent are merely copies of naturally occurring microorganisms with some modification to limit their ability to reproduce in the event they escape from the laboratory into the environment.

[6] *Laboratory Corporation of America v Metabolite Laboratories*, 548 U.S. (2006) http://www.supremecourt.gov/opinions/05pdf/04-607.pdf. "for example by forcing researchers to avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, and by requiring the costs of using the patented information, sometimes prohibitively so."

[7] North American Free Trade Agreement entered force on January 1, 1994.

[8] The United States and Australian Free Trade Agreement (USFTA) is one example. It became operational on January 1, 2005. One of its key objectives was to modify the Pharmaceutical Benefits Scheme (PBS), a uniquely Australian system that has operated since 1945 providing the Australian government with a regulatory mechanism for making medicines affordably available to Australians, to the advantage of the U.S. pharmaceutical industry. See Drahos, P., Lokuge, B., Faunce, T., Goddard, M. and Henry, D. "Pharmaceuticals, Intellectual Property and Free Trade: The Case of the US-Australia Free Trade Agreement", *Prometheus*, Vol 22, No. 3, September 2004.

regulatory authorities are now the subject of 'data exclusivity' rights.[9] These rights are separate from the patent system but they are closely aligned to it and so extend the effective monopoly period which pharmaceutical companies have come to enjoy. According to Prof Peter Drahos they provide a "means of creating a regulatory barrier to entry for generic companies that is independent of the patent system."[10] Drahos et al argue that U.S. pharmaceutical companies have "globally pushed" the adoption of these kinds of provisions through bilateral free trade agreements, going beyond the "benchmark principle" set by the TRIPS Agreement "to protect such data against unfair competition", so as to further restrict the ability of generic producers from fairly and appropriately competing with them.[11] What is motivating the pharmaceutical industry to push for these extensions is the dawning reality they are incapable of delivering on their promise - give us stronger patent laws and we will give you new medicines. In truth, despite the significant strengthening of patent laws since the World Trade Organization was formed in 1995, the number of new medicines has diminished. And without new medicines to provide new patent monopolies the pharmaceutical industry is turning more and more towards trade secret law in an attempt to extend their monopolies, thereby protecting them from generic competition and maintaining their extravagant cash flows.[12] It is expected that the loss of patent protection of these key drugs by 2012 will mean that $67 billion[13] will be lost and it is this loss that pharmaceutical companies are desperately trying to avoid.

Beyond these creative legal mechanisms, pharmaceutical companies are turning to biotechnology. Increasingly, it is the biotechnology start-ups which grabbed the headlines in the late 70s and early 80s, like Genentech and Chiron, that have been acquired by Swiss based pharmaceutical giants, F Hoffmann La Roche and Novartis. These immensely wealthy multinational pharmaceutical companies are relying on biotechnology, in part, because the patents which have been granted to their biotechnology subsidiaries give them enormous control of the world's naturally occurring genetic and protein resources. Importantly, these gene and protein patents give them an ability to control of the new wave of biologic medicines and, most importantly, the right to extract an economic rent from anyone who might be able to invent anything using these resources. In effect, these companies are like land barons - extracting rents from those that work the resources they control without having to do any of the real work. And who are the new tenant farmers? Publicly funded universities and research institutes. Ironically, it is the public who not only pay for the research to discover the naturally occurring genetic and protein resources but who also pay for the results of that research, the invented processes which produce these biologic medicines, genetic tests and, hopefully, gene therapies. The double-dipping is easily

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[9] http://www.time.com/time/politics/article/0,8599,1931595-1,00.html

[10] Op cit, 8.

[11] Although a data exclusivity provision (section 25A) was inserted into the *Therapeutic Goods Act, 1989* in 1998, the USFTA provided a mechanism to introduce further restrictions on the access and use of such data.

[12] Barbara Martinez and Jacob Goldstein, *Big Pharma Faces Grim Prognosis*, Wall Street Journal, December 6, 2007.

[13] *Ibid.*

achieved. After all, who was it that gave Amgen the biological material that enabled its scientists to decode the amino acid sequence of erythropoietin and obtain patents over the human erythropoietin gene? Dr Eugene Goldwasser. And who was it that employed him? The University of Chicago. And where did he get the biological material from? According to an obituary published in the New York Times, it came from "a foot-square package wrapped in brightly colored silk" containing dried human urine.[14] The problem is that Dr Goldwasser did not invent anything. For a start, erythropoietin is a human protein. Its existence was known. That it was extractable from human urine was known. That it could be used as a therapeutic was known. The problem was that there was no known process for its mass production. But mass production was possible, as the process developed by Stanley Cohen and Herbert Boyer in the early 70s, showed.[15] All that was missing was the genetic code for the human erythropoietin gene. Dr Goldwasser merely supplied the dried concentrated human urine to Amgen. In return he was made a member of its scientific advisory board. Then by subsequently completing the amino acid code, a result which he contributed to, Amgen was able to locate the human erythropoietin gene. This was a process of discovery. It was not a process of invention. And the so-called biologic medicine invented by Dr Goldwasser, well, that was human erythropoietin sold to hospitals around the world as Epogen. And who made all the money? Amgen.

Another example of this genetic misappropriation has recently occurred in Australia. The human gene in question is called 'SCN1A' and mutations to this gene have been linked to severe myoclonic epilepsy, known as Dravet syndrome, in infants. The research that led to the discovery of that link was publicly funded. It was performed by leading scientists from Australian universities and a teaching hospital. The result of that research was then sold to an Australian biotechnology start-up company. That company then applied for Australian public funding specifically to develop a genetic test. It received nearly $1 million dollars from the Australian people. Subsequently, this company developed a SCN1A genetic test which it licensed to another Australian company called Genetic Technologies. This is the same company that was licensed by Myriad to exploit its BRCA 1 and BRCA 2 genetic tests. As a result of this license and the price of the genetic test, one of Australia's main childrens' hospitals cannot provide the test because it cannot afford the price demanded by Genetic Technologies.[16] And, sadly, a genetic test could be manufactured by the hospital in-house if only there was no patent on the SCN1A gene mutations.

There are many other examples and those interested to learn more can read my submissions to Australian Senate Community Affairs References Committee's

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[14] Andrew Pollack, *Eugene Goldwasser, Biochemist Behind an Anemia Drug, Dies at 88*, New York Times, December 20, 2010.

[15] Stanley Cohen et al "Construction of Biologically Functional bacterial Plasmids in Vitro", *PNAC*, 70 (11), November 1973, pp 3240-3244.

[16] Julie Robotham, *Sick babies denied treatment in DNA row*, Sydney Morning Herald, November 29, 2008.

Inquiry into Gene Patents[17] or my book *Gene Cartels, Biotech Patents in the Age of Free Trade.*[18]

The Patent Amendment (Human Genes and Biological Materials) Bill, 2010.

On a sunny spring morning on the grounds of Australia's Parliament House nearly 100 Members of Parliament, Senators, their advisors and staff, together with a large media contingent, gathered on one of the many the internal lawns to hear Mrs Sarah Murdoch, patron of the National Breast Cancer Foundation, Prof Ian Olver, chief executive officer of Cancer Council Australia, the country's peak cancer body, along with Senators Bill Heffernan and Nick Xenophon and MPs, Ms Melissa Park, Mr Peter Dutton (also Shadow Minister for Health) and Mr Rob Oakeshott speak in support of a Bill to ban patents on naturally occurring biological materials.[19]

A few days later the *Patent Amendment (Human Genes and Biological Materials) Bill*, sponsored by Senators Heffernan, Helen Coonan, Xenophon and Rachel Siewert, who, incidentally, had chaired the Senate's Gene Patent Inquiry, was introduced into the Australian Senate. In February 2011 the same Bill was introduced into the Australian House of Representatives. It is now under review by the Australian Senate Legal and Constitutional Affairs Legislation Committee.[20]

It is not a secret that I drafted both the Bill and the Explanatory Memorandum.

The Bill's Explanatory Memorandum states:

> The purpose of this Bill is to advance medical and scientific research and the diagnosis, treatment and cure of human illness and disease by enabling doctors, clinicians and medical and scientific researchers to gain free and unfettered access to biological materials, however made, that are identical or substantially identical to such materials as they exist in nature. These biological materials even if they have been isolated, purified or synthetically made have not been transformed from products of nature into products of humankind.

The Bill's key provision is section 18(2)(b). It reads as follows:

> (2) The following are not patentable inventions:
>
> (a) ....
>
> (b) biological materials including their components and derivatives, whether isolated or purified or not and howsoever made, which are identical or substantially identical to such materials as they exist in nature.
>
> (5) ***biological materials***, in section 18, includes DNA, RNA, proteins, cells and fluids.

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[17] http://www.aph.gov.au/senate/committee/clac_ctte/gene_patents_43/submissions/sub04a.pdf

[18] http://www.amazon.co.uk/Gene-Cartels-Biotech-Patents-Trade/dp/1847208363

[19] http://www.theaustralian.com.au/national-affairs/sarah-murdoch-urges-gene-control/story-fn59niix-1225954938553

[20] http://www.aph.gov.au/senate/committee/legcon_ctte/patent_amendment/index.htm

So far 110 submissions have been received, including from the American Intellectual Property Law Association (AIPLA), the Biotechnology Industry Organization (BIO), Pfizer, Abbott Laboratories, Baxter Healthcare, Bristol-Myers Squibb, Merck Sharp and Dohme, Merck Serono, GlaxoSmithKline, Eli Lilly, Roche, Sanofi Aventis and Amgen. Thus, the Bill is being closely monitored by those who believe they have the most to lose if the correct legal balance is returned to the Australian patent system.

The Bill does no more than enforce a 400 year old principle of patent law - that a patent monopoly be granted in return for the public disclosure and working of an 'invention', yet each of these U.S.-based organizations have filed submissions against the Bill. Their arguments are very similar.

First, there is no evidence that patents stifle research in Australia. That's not true.

Secondly, the Bill is too broad, is vague and ambiguous and may eliminate patents for therapeutic products. That's not true either.

Thirdly, the Bill will not prevent patents on methods and as a result "the proposed Amendment appears to do little to address the fundamental concerns underpinning the debate on access to genetic testing in Australia". That's also not true.

Finally, the Bill violates TRIPS, the AUSFTA and is "inconsistent with the expansive patent protection afforded to biological materials in all other industrialized countries..". Another untruth.

My answer to each of these four key objections is straight forward.

The issue, and the one which they have not addressed in their submissions, is the threshold of invention. The Bill does no more than seek to enforce the law as it should be applied in regards to that threshold. The fact that patent law as is currently practiced is of questionable legality is a reflection of the breakdown in regulatory governance, not a reflection on the correctness of that principle.

That principle has stood for nearly 400 years. It is the foundation stone of all patent laws in all countries. For more than 150 years the U.S. Supreme Court has upheld this principle in its precedents. And either this principle is meaningful or it is not. If it is, then it must be rigorously defended and maintained.

Any suggestion that the Bill violates TRIPS or the AUSFTA is untenable. The key word in both article 27.1 TRIPS and section 17.9.2 AUSFTA is 'invention'. Both of these provisions require patents be granted only for 'inventions' and then only if the invention meets the other thresholds of patentability, namely, novelty, inventive step and usefulness. Indeed, it is arguable that the EU's Biotechnology Directive violates TRIPS because it mandates EU member countries to treat isolated biological materials as 'inventions' when the truth is that no one invented them.

The Bill will not prevent the patenting of modified biological materials when the modifications can justify their treatment as products of humankind and not as products of nature. Thus, the Bill does no more than apply the law as applied by the U.S. Supreme Court in the famous case of *Diamond v Chakrabarty* 447 U.S. 303 (1980).

It is not the objective of the Bill to exclude from patentability:

(a) products, process or methods that make use of, or include as a component or components, naturally occurring biological materials, even if identical or substantially identical to any that exist in nature, in such things as diagnostics, pharmaceuticals, therapeutic products or methods, treatments and cures; and,

(b) biological materials derived from naturally occurring biological materials provided such derivatives are not (a) identical or (b) substantially identical to any that exist in nature; and

(c) naturally occurring biological materials which have been modified, genetically or otherwise, so that in their modified form the way they function is so changed when compared to their pre-modification state that they can no longer be considered to be identical or substantially identical to any that exist in nature.

Any of these things will fall outside of the scope of the prohibition in section 18(2)(b). Accordingly, as patentable subject matter they will, subject to satisfying the residual prerequisites of patentability prescribed in sections 18(1)(b) and (c) and meeting all other legislative and regulatory requirements, be the subject of an Australian patent.

Although the Bill does not contain any language along these lines, the term 'substantially identical' infers this result.

'Substantially identical'

The term 'substantially identical' is not new to intellectual property law. It is used extensively in the *Trade Marks Act 1995* (sections 23, 44, 60, 102, 120, 122, 124, 133, 146 and 230). Furthermore, it is undefined in that Act. Even so, the term has come to be understood, through a process of judicial interpretation, to mean something specific in the context of trade mark law. The term 'substantially identical' is, for instance, used in section 44 of that Act as a prerequisite to registration. Therefore, it is a matter of consideration at the application stage that a trade mark examiner must exercise discretion in deciding if an application for a registered trade mark is 'substantially identical' to a pre-existing registered trade mark. The examiner does so by applying a body of judicial-made law which has built up over time.

Similarly, it is open for an Australian court to interpret the term 'substantially identical' in the context of section 18(2)(b) by drawing a distinction between a naturally occurring biological material and one that has been modified so that it can no longer be said to be a product of nature but, instead, be a product of humankind. Indeed, the U.S. Supreme Court made such a distinction in *Diamond v Chakrabarty* in relation to a genetically modified bacterium that was able, due to human intervention, to degrade crude oil. The bacterium in issue was naturally occurring but the genetic modifications performed by scientists so changed it that it was, in its genetically modified form, able to perform a function completely unknown in nature. In this circumstance the Court concluded that the genetically modified bacterium was patentable subject matter under U.S. patent law because it was "new with markedly different characteristics from any found in nature and one having the potential for significant utility".

While it is currently the case that there is no Australian court authority equivalent to *Diamond v Chakrabarty* and accepting that it is matter for the

Australian courts to interpret and apply Australian law, it is equally true that the High Court of Australia has referred, on occasion and when necessary, to the decisions of foreign courts, particularly those of the U.S. Supreme Court, as an aid to the interpretation of Australian intellectual property law.

It may be argued that absent a statutory definition of 'substantially identical' there is some uncertainty in how the Australian courts will interpret and apply section 18(2)(b), however, the counter to that argument is that there already exists a body of law, albeit foreign, which provides guidance on point and which, with respect to those whose mistrust of Australian courts is implied by their concern, has been applied both by other foreign courts and very recently by the U.S. Department of Justice (acting on behalf of the U.S. government), in submitting to the U.S. Court of Appeals for the Federal Circuit that isolated genomic DNA is not patentable subject matter under U.S. patent law.

Modified biological materials are not excluded by the Bill

This distinction, made possible by the application of this judicial test, is important as today many pharmaceuticals and vaccines are derivatives of naturally occurring biological materials.

Example 1. NovoLog (a human insulin derivative product)

An example is the pharmaceutical NovoLog. NovoLog is a trademark owned by Novo Nordisk, a Danish biotechnology and pharmaceutical company, and applied to a pharmaceutical preparation containing two modified forms of human insulin, one of which currently is the subject of a U.S. patent application (U.S. 2007190159).

The Bill, had it been enacted in the 1970s, would have prevented the patenting of human insulin *per se*, something which Genentech, a U.S. corporation based in Silicon Valley, was able to achieve in Australia under the policy pursued by IP Australia. It would not, however, prevent the patenting of the insulin analogue under consideration. This is because the Novo Nordisk insulin is markedly different from normal human insulin because it performs in the human body in a way that is superior to human insulin. Accordingly it is not 'substantially identical' to human insulin, despite the fact that at an amino acid level there is only one amino acid difference between the two forms of insulins.

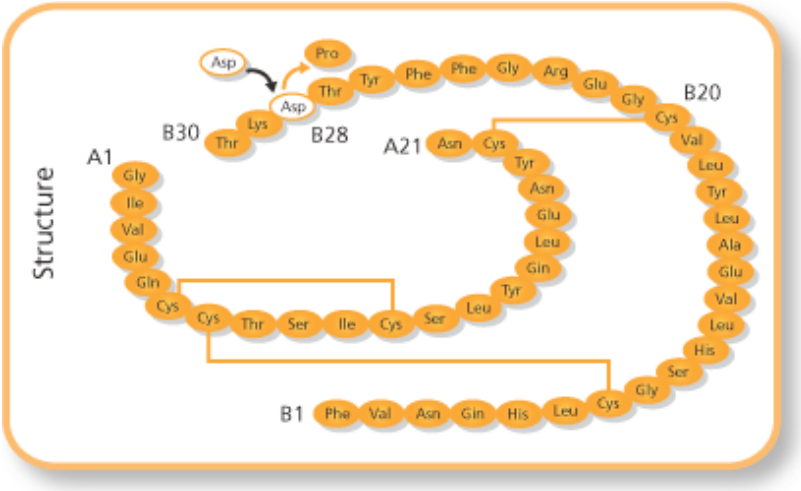

Fig. 1: Amino acid structure of Novo Nordisk's modified human insulin

That difference, at position B28 (the substitution of proline with aspartic acid), is what gives the Novo Nordisk human insulin its enhanced performance, namely, by making it faster acting in the human body than normal human insulin. This enhanced performance is the kind of 'significant utility' which the U.S. Supreme Court was referring to in *Chakrabarty*. It also means that it is 'markedly different'.

Only biological materials (whether isolated or not) as exist in nature are excluded by the Bill

However, where a naturally occurring biological material has not been modified, other than by its removal (or isolation) from its naturally occurring environment, the Bill does prevent its patenting. This is because the biological material, whether it be a human gene or protein or some other kind of biological material, is not markedly different from any found in nature. Moreover, the biological material has no material point of distinction, either structurally or functionally, to the biological material in its natural environment. The mere isolation of a biological material simple changes its state but it does not change what it is or what it does.

It is true, however, that in an isolated form the biological material is not identical to the biological material as it exists in its natural environment. Indeed, the act of isolation itself necessarily involves some modification to the structure of the biological material, but what is important to appreciate is that that kind of modification does not satisfy the judicial test in *Chakrabarty*. As already stated, the modification does not change what it is or what it does.

Example 2. In vivo mutations and polymorphisms in the 17q-linked breast and ovarian cancer susceptibility gene (breast and ovarian cancer gene mutations)

Certain genetic mutations in the human gene BRCA 1 have been linked to breast and ovarian cancers in humans. These genetic mutations are naturally occurring. Their isolation did not materially change them. It merely removed them from the patients from which they were identified.

Even so, they were made the subject of Australian patent 686004. The patent was granted by IP Australia to Myriad Genetics, a U.S. corporation based in Utah.

Claim 1 of the Australian patent defines the alleged invention to be:

> An isolated nucleic acid coding for a mutant or polymorphic BRCA1 polypeptide, said nucleic acid containing in comparison to the BRCA1 polypeptide encoding sequence set forth in SEQ.ID No:1 one or more mutations or polymorphisms selected from the mutations set forth in Tables 12, 12A and 14 and the polymorphisms set forth in Tables 18 and 19.

It needs to be understood that a patent claim defines the legal boundaries of the patent monopoly. This means that the possession, use, making, sale or dealing with any biological material that comes within the boundary of claim 1 amounts to an infringement of the patent. It does not matter how the biological material is made. It does not matter how the biological material is used. The patent monopoly defined here by claim 1 applies to the biological material *per se*. This gives the patent owner the legal right to sue the infringer for damages, an

account of profits and injunctions extending to the destruction of any infringing items. The patent owner is also awarded legal costs in the event that the infringement is proven.

I will now explain (and I have deliberately colour coded the relevant words and phrases to assist) what this claim means.

First, the word 'isolated' in the context of the claim means that the genetic mutations defined in Tables 12, 12A and 14 (which are found in the specification of Australian Patent 686004) have been physically removed from breast cancer patients in which they were identified. That is what 'isolated' means in this context, nothing more. It should be noted that Myriad's scientists, therefore, did not invent nor create these genetic mutations. They merely discovered them. More importantly, in isolating them they did not modify them structurally in any material way.

Secondly, the term 'nucleic acid' means DNA. Again Myriad's scientists did not invent nor create this DNA.

Thirdly, the phrase 'coding for a mutant or polymorphic BRCA1 polypeptide' refers to the mutant BRCA protein. As DNA is the biological repository of information which the human body uses to manufacture proteins you can consider the DNA to be the blueprint while the protein is the resulting physical manifestation. The word 'coding' means that the DNA houses the information for a specific protein. The two, the gene and the protein coded by that gene, are therefore inextricably linked.

Finally, the phrase 'one or more mutations or polymorphisms selected from the mutations set forth in Tables 12, 12A and 14' means those mutations as defined in the tables set forth in the patent. If we look at Table 12, for example (reproduced below), we can see what these are.

TABLE 12

Predisposing Mutations

Patient	Codon	Nucleotide Change	Amino Acid Change	Age of Onset	Family History
BT098	1541	GAG → TAG	Glu → Stop	39	-
OV24	819	1 bp deletion	frameshift	44	-
BT106	1708	GCG → GAG	Ala → Glu	24	+
MC44	1775	ATG → AGG	Met → Arg	42	+
17764	958	4 bp deletion	frameshift	31	+
19964	958	4 bp deletion	frameshift		+*

Fig. 2: Table 12: BRCA 1 genetic mutations linked to breast and ovarian cancer

The table contains six different genetic mutations, *each* of which has been identified from human body samples provided by six different breast cancer patients. This is clear from the heading to column 1 - 'patient'. The other five columns refer to (a) the location of the mutation on the respective patient's BRCA

gene, (b) the genetic sequence of the mutation (because it refers to the nucleotide change), (c) the nature of the protein mutation (because it refers to amino acid change), (d) the patient's age when diagnosed with breast cancer and (e) any relevant family history.

On the basis of this data alone it is fair to conclude that the Myriad scientists described as 'inventors' did no such thing.

Medical and scientific uses of biological materials (whether isolated or not) as exist in nature are not excluded by the Bill

Staying with Example 2 it should be noted that the BRCA 1 Patent is actually made up of 30 patent claims in total. And while there are 6 claims to either isolated BRCA 1 genetic mutations and/or purified BRCA 1 mutant proteins, the remaining 24 claims are to various products, process or methods which either contain the isolated biological materials of claim 1 or make use of them in some way.

For example there is claim 17, which states:

> A method for diagnosing a predisposition for breast and ovarian cancer in a human subject which comprises determining whether there is a germline alteration in the sequence of the BRCA 1 gene in tissue sample of said subject compared to the nucleotide sequence set forth in SEQ:ID 1 or a wild-type allelic variant thereof, said alteration indicating a predisposition to said cancer being selected from the mutations set forth in Tables 12, 12A and 14.

In layman's language this claim defines the patent monopoly to be *any* method (not a specific diagnostic method) of determining if a patient's genome contains one or more of the genetic mutations defined in Tables 12, 12A and 14.

Of course this raises the question: is the use of these genetic mutations in this way *truly* inventive? In other words, does using the materials in any diagnostic method involve an i*nventive step*? And while *inventive step* is a further prerequisite of patentability it must be understood that it is separate to the prerequisite which the Bill deals with, namely, patentable subject matter.

A valid patent must satisfy all four prerequisites. These prerequisites, as provided in section 18(1) *Patents Act, 1990*, are (a) patentable subject matter (b) inventive step (c) novelty and (d) utility. The Bill deals *only* with the first of these.

Nevertheless, assuming that claim 17 satisfies all four patentability prerequisites it would be a valid patent claim, giving the patent owner a 20 year monopoly over *any* breast and ovarian cancer gene testing anywhere in Australia.

Improving access to genetic testing

Opponents argue that the Bill does nothing to improve patient access to genetic testing. But they are wrong for the following reasons:

First, the Bill prevents the monopolisation for 20 years (a very significant period of time) of the fundamental raw ingredients of these genetic tests: the actual genetic mutations which, we all know, are not invented. This frees up other scientists and doctors to use these biological materials to make new and inventive medical and scientific products, processes and methods using these materials in laboratories and for clinical use.

Next, the Bill prevents the privatisation of genetic sequence information - information which belongs to humanity and is not the product of human ingenuity but is the product of human evolutionary and natural processes. In so doing the Bill enhances access to genetic testing by ensuring that genetic information is not controlled by any one individual, company or organisation.

Finally, it is true the Bill is only one of several measures needed to be taken in order to improve patient access to genetic tests, but that does not undermine the rationale for it. It may be only one of the pieces in the puzzle needed to solve the problem of patient access to genetic testing but it is an important piece nevertheless. Of course, more needs to be done to improve patient access to genetic testing and, while other policy and legislative changes are required, this Bill is an integral part of the solution.

Patenting of products, processes or methods that make inventive uses of biological materials (including those naturally occurring).

Opponents argue the Bill will remove the incentive to invest in medical inventions such as the Gardasil vaccine. This is not true. The Bill will do the precise opposite.

The Bill will vastly improve the research and development landscape for medical, scientific and biotechnological inventions by making it easier and less risky for Australian researchers, clinicians and pharmaceutical/biotechnology companies to gain free and unfettered access to biological materials so that they can develop cheaper, more efficient and more innovative vaccines, medicines, diagnostics, treatments and therapies and the processes of their manufacture.

The Bill does not prevent the patenting of end products such as vaccines and diagnostics. To begin with, these end products are not naturally occurring biological materials. Pertinently, they are not 'substantially identical' to naturally occurring biological materials. A vaccine does not consist only of a naturally occurring biological material *per se*. It is made up of a variety of components. True it may be that one of these will be a biological material that is either identical or substantially identical to what exists in nature, but the vaccine itself, as a whole, is materially different.

A vaccine, apart from being structurally different to naturally occurring biological materials, also functions in a way that naturally occurring biological materials do not. The effect of a vaccine is to *induce* an immunological reaction so that antibodies produced in response to the vaccine create a level of immunity to the antigen which the vaccine is directed to. The level of immunity can vary. It can be temporal or permanent. But, whichever, this effect is induced by effect of the vaccine as a *whole*, and not merely by one of its components.

The Bill does not prevent the patenting of processes for the manufacture of a naturally occurring biological material even if that material is identical or substantially identical to one that exists in nature. Therefore, the Bill focuses the incentive to innovate on the process rather than the end result, the product of that process. Indeed, it is precisely this focus which contributed to the industrialisation of Germany in the 19th century and which gave German chemical companies the massive comparative advantage in synthetic dyes and chemicals, leading to the first modern pharmaceuticals, such as Aspirin in 1899. By WWI German chemical companies dominated world markets. This domination

was broken only when the governments of the UK and the US either banned patents on chemical substances (the UK response bringing UK patent law into line with German patent law) or confiscated German owned chemical patents giving them to their own fledgling chemical companies (the US response). In both instances these policies had the desired effect and gave their own domestic chemical industries a shot in the arm. The same is true today for biological materials. By focusing the innovation incentive on new and inventive *processes*, the production costs of biological materials needed for new vaccines, medicines, diagnostics, treatments and therapies will fall as the supply increases. Importantly, the Bill will give Australian biotechnology companies and research institutes a much needed shot in the arm - a chance to compete - in producing new and innovative scientific and medical products that may be manufactured in Australia and exported all over the world.

Example 3. The Gardasil vaccine

The Gardasil vaccine is protected not by one patent but by a series of patents. This is typical of most medical inventions.

One of these patents is an Australian patent. Its serial number is 682092 and its title is: “Modified Papilloma Virus L2 Protein and VLPs Formed Therefrom”.

As you will have gathered from its title the patent is about a biological material - a protein. But what is important to note is that there is much more to the patent than that. The patent consists of 11 claims. Each of them set out the legal boundaries of the patent monopoly. And each of them is separate and separately assessed in terms of its validity and infringement. In essence the patent monopoly consists of a web of associated and connected inventions defined by the 11 separate claims. As a result it is possible for one or more of them to be invalid without invalidating the entire patent or, more importantly, the claim to the Gardasil vaccine itself. Turning to the patent I will explain how the Bill will not adversely impact on the Gardasil vaccine.

The principal claim of the patent is claim 1. It is the broadest claim but it is separate to, for instance, claims 5 to 7 which are claims to methods of *producing* a protein of claim 1. Again it is separate to claims 9 and 10 which are to vaccines that *include* a protein of claim 1 *as a component*. But before turning to claims 5 to 7 and claims 9 and 10, let us begin by examining claim 1.

Claim 1 reads as follows:

> A papilloma virus L2 protein which does not bind DNA or which has a substantially impaired ability to bind DNA compared to wild type papilloma virus L2 protein.

That protein - the papilloma virus L2 protein - as defined in that claim, is the alleged ‘invention’. The relevant question is this: is the papilloma virus L2 protein defined by that claim either (a) identical or (b) substantially identical to a protein that exists in nature?

If the answer is in the affirmative then it will not, according to the Bill, be patentable subject matter. And why, if that were the case, should it be? There is no act of invention in the discovery of such a protein. The protein is little more than an artefact of nature. After all gold, uranium, cotton and wool are not inventions and no one has the right to claim to have invented these natural

artefacts even if they were the first to discover them or learn to use them in some inventive way. Sure, there may have been patents in the past over the extraction of gold, the processing of uranium, the spinning of cotton or the weaving of wool but not over gold, uranium, cotton or wool themselves.

In the same way, making a protein of claim 1 synthetically through some inventive *process* or making a *vaccine* containing the protein is different to the actual protein itself. Processes and products are not what the Bill is aimed at. These are not biological materials as exist in nature and it is absurd for anyone to argue that they are.

That said, it is clear from the definition of the protein of claim 1 that the inventors, Prof Ian Frazer and Prof Jian Zhou, recognising that the papilloma virus L2 protein is a naturally occurring protein, attempt to distinguish the protein of claim 1 from the "wild type papilloma virus L2 protein". The key term here is: "wild-type". The term imputes a distinction, which the inventors say is relevant to the validity of their invention, between the naturally occurring protein and the protein which is the product of the processes defined in claims 5 to 7.

Now whether there is, as a matter of objective scientific fact, a material difference between the two proteins is a matter of independent expert analysis and opinion, but regardless of whether they are or they are not, the incontrovertible truth is, the claims to the processes (claims 5 to 7) and the Gardasil vaccine (claims 9 and 10) are not touched by the Bill. In other words, even if claims 1 to 4, 8 and 11 (which are claims to a modified papilloma virus L2 protein) are not valid because they are found to be identical or substantially identical to the protein as it exists in nature, the manufacture of the proteins and their use as a component in the Gardasil vaccine would not be prevented from patenting by this Bill. At the end of the day the patent claims to the Gardasil vaccine would be untouched.

How many patents of this kind are out there?

In a word, thousands. Unfortunately it is impossible to give an exact number of how many have been granted or applied for in Australia because the data is not readily available, but an approximate number, as at February 16, 2009 and based on a survey using a blend of patent classification statistics and search criteria, is 15,000.[21]

What's happening with the Bill?

The Bill has been introduced into both Houses of the Australian Parliament. It is currently under review by the Senate Legal and Constitutional Affairs Legislation Committee. Submissions have closed and public hearings will be held in late April. The Committee is due to report to the Parliament by June.

It is difficult to predict whether the Bill will be passed into law. This is because of the level of opposition coming from virtually all quarters. The objectors include patent attorneys, biotechnology and pharmaceutical companies, medical and scientific research institutions, professional scientific associations, private research institutions, academics, scientists and specific medical condition associations. The opponents, however, are relying on fear to paralyse law makers.

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[21] Second Submission #4 (Luigi Palombi) to the Australian Senate Community Affairs References Committee's inquiry into Gene Patents: http://www.aph.gov.au/senate/committee/clac_ctte/gene_patents_43/submissions/index.htm

This is a gamble. While the 'sky-falling-in' approach may succeed it is possible that it may also make law makers question the bona fides of those who oppose the Bill. There is a distinct lack of substantive argument to support the scenario they paint. Indeed, the Bill will not prevent the patenting of new and inventive applications, including in products and processes, of these materials. If law makers are prepared to get their hands dirty and figure out where the truth lies then there is a much better chance the Bill will survive and become law.

Is TRIPS a problem?

In one word: No. Article 27.1 mandates that patents be made available only for 'inventions' and only if those inventions are novel, involve an inventive step and have a useful or practical application. The fact is that isolated biological materials are discovered. They are not invented. And where the line between discovery and invention is to be drawn when it comes to natural phenomena which have been modified, the settled and well respected U.S. Supreme Court decision in *Diamond v Chakrabarty* provides guidance.

Does what happens in Australia matter to the rest of the world?

Yes. Australia is part of an international community and its actions, and the reasons for its actions, can be influential on its major trading partners and its neighbours.

Conclusion

This Bill will not resolve all of the problems which currently plague Australia's patent system. And it's not designed to. It is a nuanced, controlled and expertly crafted response to a specific problem in Australia's patent system. It is like a surgeon's scalpel removing a festering boil. That it prevents the patenting of biological materials which exist in nature is an achievement in itself. It puts to an end, once and for all, any suggestion that the mere isolation of a biological material from its natural environment transforms that material from a product of nature into a product of invention. But it does more. It also prevents the patenting of modified biological materials when those modifications are so minor, insignificant or immaterial that they cannot be said to transform the biological material into being an 'invention'.

The Bill will return the incentive to undertake research and development in Australia so that Australian scientists can help Australian companies produce new and much needed medicines, diagnostics and therapeutics. In so doing the Bill will reduce the cost of research by giving Australian scientists free and unfettered access to biological materials which no one invented. It will remove the legal handcuffs, enabling them to pursue their research without fear of patent litigation. And, most importantly, it will refocus innovative competition to a higher standard. One of the purposes of Australia's patent system is to reward invention, true invention.