THE AUSTRALIAN NATIONAL UNIVERSITY

REGULATORY INSTITUTIONS NETWORK (RegNet)
Centre for the Governance of Knowledge and Development

H.C. Coombs Building Extension
Cnr Fellows & Garran Roads
The Australian National University,
Canberra, ACT, 0200
Australia

http://www.regnet.anu.edu.au

SUBMISSION 1

Thursday, 24 February 2011

Ms Julie Dennett
Committee Secretary
Senate Standing Committee on Legal and Constitutional Affairs
Parliament House
CANBERRA 2600

Dear Ms Dennett

Inquiry into the Patent Amendment (Human Genes and Biological Materials) Bill 2010

I am writing to you in reply to the Committee's invitation, extended to me by letter dated December 9, 2010, to make a "contribution" to the above mentioned Inquiry. I do so on my own behalf.

I am the principal drafter of the Bill and the Explanatory Memorandum.

1) Objective of the Bill

The objective of the Bill is to assist in the recalibration of Australia's patent system.

It does so by strengthening the prerequisite of patentable subject matter (section 18(1)(a) and section 18(2) *Patents Act, 1990*) in regard to the patenting of biological materials, specifically, by making it impossible for patent monopolies to be granted over: (a) products, processes or methods that are illegal, immoral, disreputable or otherwise injurious to Australian society or the economy; and, (b) naturally occurring biological materials.

First, the amendment to section 18(1)(a) overturns two longstanding but, problematic, Full Federal Court decisions. They are *Anaesthetic Supplies Pty Ltd v Rescare Ltd* [1994] FCA 1065 and *Bristol-Myers Squibb Co v F H Faulding & Co Ltd* (2000) FCR 524. In so doing the Bill restores the original intent of the *Patents Act, 1990,* and one that goes to the heart of Australian patent law, by preventing the grant of patents over subject matter which would be "contrary to the Law, nor mischievous to the State, by raising Prices of Commodities at home, or Hurt of Trade, or generally inconvenient". This aspect of the Bill is designed to re-impose on the courts an obligation to inquire into the suitability, for the grant of a patent monopoly, subject matter that may be illegal, immoral, disreputable or otherwise injurious to Australian society or the economy and reinstate their power to strike these down *ab initio*, as if they had never existed.

Secondly, the amendment to section 18(2) reverses the aberrant policy, adopted by IP Australia about 30 years ago, leading to the grant of thousands of patent monopolies and which, absent the Bill, will lead to thousands more over naturally occurring biological materials. These materials include human genes and proteins but are not limited to them. Indeed, any biological material that is either (a) identical, or, (b) *substantially* identical, to *any* that exist in nature will be prohibited from patentability. The prohibition includes their *derivatives* and *components* that are (a) identical or (b) substantially identical to *any* that exist in nature.

In short, this aspect of the Bill seeks to stop the patenting of naturally occurring things which no one invented and with respect to which any human modification to them is so insignificant that any structural change caused by that modification is immaterial in regard to its pre-existing, natural, function. For example, human insulin *per se*, a natural protein, or the human gene which codes for it will no longer be patentable subject matter.

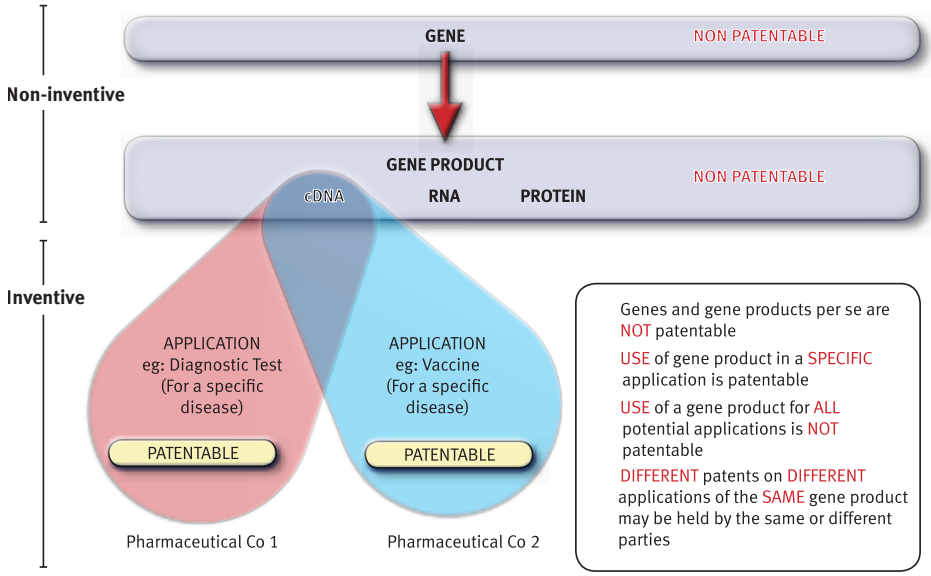

Fig. 1: Diagram depicting the narrow scope of the prohibition in section 18(2)(b) in relation to DNA

2) The narrow scope of exclusion contemplated by the Bill

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 be, subject to satisfying the residual prerequisites of patentability prescribed in sections 18(1)(b) and (c) and meeting all other legislative and regulatory requirements, 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). However, it is not defined in that Act. And even so the term has come to be understood, though 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 register 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, The Commissioner of Patents v Chakrabarty* 447 U.S. 303 (1980) 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 interpretation of Australian intellectual property law.

While 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), 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, indeed, 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.

3) 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.

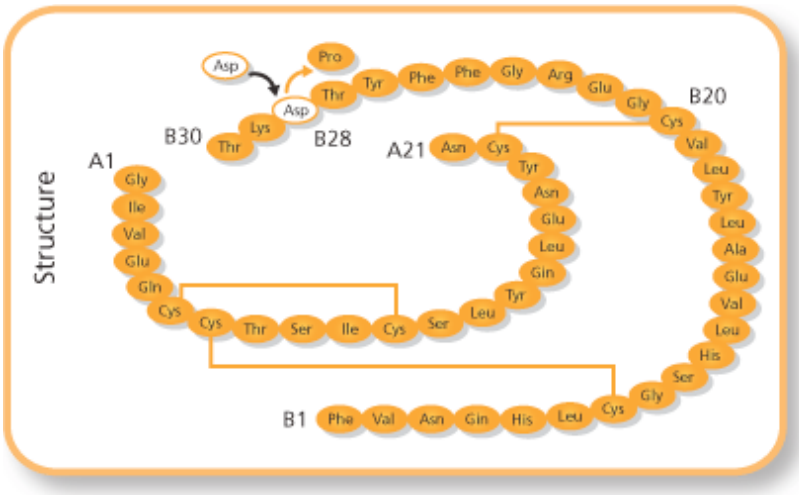

Fig. 2: Amino acid structure of Novo Nordisk’s modified human insulin

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'.

4) 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 in how it functions, 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 nor 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 nor 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.

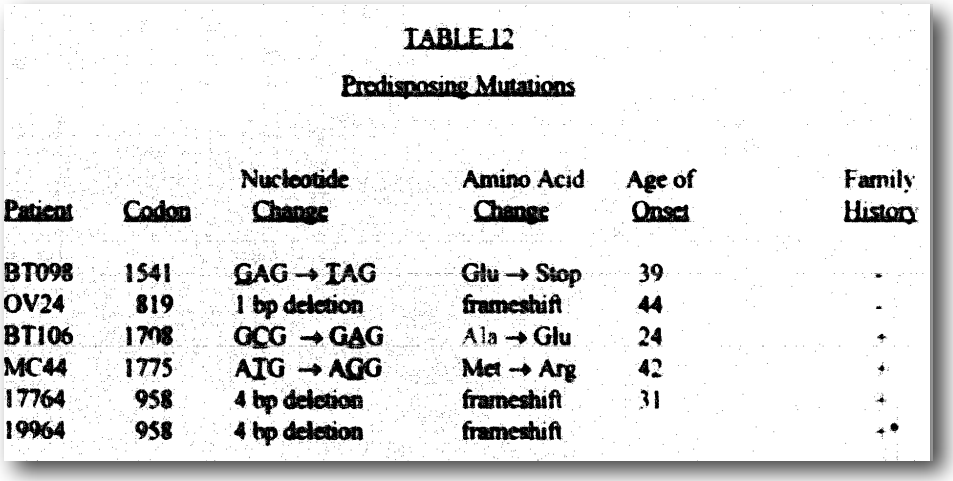

TABLE 12

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. 3: 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.

5) 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 *inventive 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.

6) 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, 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.

7) Patenting of products, processes or methods that make inventive uses of biological materials (including 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 to an antigen 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) 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 Gar-

dasil 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.

8) 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 Australia 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.

9) Declaration of Interest

Finally, I wish to declare to the Committee that I have no interest, direct or indirect, financial or otherwise, in the subject of this Inquiry or in its results. Neither I, nor any member of my direct family, nor any corporate vehicle in which my direct family owns or controls, has any shares in any biotechnology company or has any interest in any organisation that may directly or indirectly benefit from patents of the kind which may be impacted by the Bill (should it become law). I am not a member of a patent attorney firm nor do I have any interest, actual or contingent, of any kind in such firms. Indeed, I have nothing to fear nor favour from the Bill nor the outcome of this Inquiry.

Yours sincerely,

Luigi Palombi LL.B (Adel), B.Ec (Adel), Ph.D (UNSW) and Adjunct Professor of Law, The University of Sydney