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## The Patenting of Biological Materials

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Medical scientists and researchers both at universities and in commercial laboratories are today facing a tidal wave of patents. These patents claim, as 'inventions', biological materials which are substantially identical to or indistinguishable from naturally occurring biological materials. Examples include erythropoietin, a human protein that regulates the production of red blood cells, and hepatitis C virus, a viral agent that causes a form of chronic hepatitis in humans called hepatitis C.

The problem which Australian scientists face is that they must first have the approval of the patent owner before they can conduct research using these biological materials and negotiating for the necessary authority has become expensive, technical and onerous. Furthermore, patent owners that do give their authority, usually stipulate that any intellectual property developed with the use of those materials must be forfeited to or controlled by the patent owner. The result is that the very incentive which the patent system is supposed to promote in innovative solutions to human disease and illness is actually being destroyed or rendered illusory. Unfortunately, even if their research is conducted in universities there is no guarantee that they and their university cannot be sued for patent infringement because in many instances they are either funded by a commercial organisation or there is a commercial objective.

Professor Baruch S. Blumberg was awarded the *Nobel Prize for Physiology or Medicine* in 1976 in recognition of his research concerning mechanisms involved in the origin and spread of infectious diseases and, specifically, for the discovery of the hepatitis B virus and for the development of methods for detection of HBV and the vaccine for HBV. In the Federal Court of Australia, in patent revocation proceedings which I brought to trial in June 1996 concerning an Australian patent granted over Hepatitis C proteins, he testified that:

I have reviewed Chiron's Australian Patent No. 624105 for the purposes of these proceedings. ... These claims represent a view in scientific thought, i.e., that knowledge of the nucleotide sequence of the virus genome, let alone part of it, tells one all that needs to be known about the functions of the proteins produced by the virus and hence all that needs to be known about the virus. I do not subscribe to this view. Such a view infers that all other information about the proteins and their effects, including post-translational changes in the gene-produced proteins, interactions of viral proteins with each other, interactions of the viral gene products with the host, the biology of the virus and its host, demonstration of effectiveness, etc. is redundant. It states in effect: "Anything that is done with the HCV virus is covered by this patent and all research and development on the virus is subservient to it." ... Based on the unusually broad nature of the patent, if I were a research director for anti-virals and had the option of working on several viruses, **the existence of this patent would weigh against my deciding to undertake HCV research.** A company, or even an academic laboratory, might well be deterred from conducting research on HCV because the patent is, in effect, intimidating.

It is important to note, that since 2001 the numbers of patents filed in Australia in the field of biotechnology (according to IP Australia's published patent statistics) have fallen by 30% while patents for pharmaceuticals have risen by 18%. I believe that one reason for this fall is due, as Prof. Blumberg warned in 1996, to the disincentive for medical and scientific research created by the grant of patents over isolated biological materials.

The central argument behind the view that isolated biological materials can be patentable 'inventions' is that they are either removed from the natural environment in which they naturally are found, such as the human body, or they have been manufactured or produced by technical means, such as with the use of recombinant methods or technologies. This step of isolating or purifying biological materials, it is argued, sufficiently distinguishes them from their naturally occurring counterparts so that they can be deemed to be 'inventions' i.e., the artificial products of human ingenuity.

This argument, however, has never been the subject of judicial scrutiny in Australia (except in the case of *Murex v Chiron* which I brought but which unfortunately settled out of court during week 9 of the trial) despite the fact that the Australian patent office commenced granting patents over isolated biological materials in the late 1980s.

It is a matter for legal argument, but in my opinion if one studies the U.S. Supreme Court's famous case of *Diamond v Chakrabarty*, one sees that the Supreme Court stipulated that only if the genetically modified bacterium displayed "markedly different characteristics from any found in nature" (see 447 U.S. 303 at 310) could it be considered to be patentable subject matter. On the facts of that case, the bacterium was able to degrade crude oil, a function for which there was no natural precedent.

*Diamond v Chakrabarty* has been universally acknowledged as the case which started the biotechnological revolution but unfortunately this is more a coincidence than substantive because the mere isolation or purification of naturally occurring biological materials cannot under any reasonable interpretation, *display markedly different characteristics from any found in nature*. Whether these materials are artificial in the sense of being 'isolated' or whether they are produced by a recombinant technology such as that pioneered by Cohen and Boyer, the simple truth is that the end products are biological materials that are identical or indistinguishable to their naturally occurring counterparts. For example, the identical nature of artificial erythropoietin to natural erythropoietin was acknowledged by the U.S. District Court for the District of Massachusetts in *Amgen v Chugai* (1989 11 U.S.P.Q.2D (BNA) 1466) where the court decided:

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

Unfortunately, the issue of whether rEPO was an 'invention' was not in issue in the case because the battle between Amgen and Chugai was: who was the first to invent rEPO? It was not in either of their interests to challenge each other with an issue that could potentially destroy their respective patents. So, absent this issue the Court simply resolved who invented rEPO first. Nevertheless, the Court's observation reinforced the point which I make: that isolated or not, erythropoietin is erythropoietin.

Eventually, the European patent equivalent of the U.S. patent that was the subject of the above case came before the House of Lords in July 2004 (See *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd and others*). In that appeal, the issue of whether there was an 'invention' or not was again not in issue, essentially for the same reasons that it has never been in issue – all parties have their own patents over isolated biological materials.

It is noteworthy that this European patent was due to expire in December 2004, but such were the economic stakes that the parties were able to justify the cost of very expensive lawyers and the valuable time of the House of Lords in the appeal even at the 11<sup>th</sup> hour. In the end, the House of Lords held that the relevant 'inventions' were all invalid because according to their Lordships (it was a unanimous decision delivered by Lord Hoffmann) rEPO, the end product of the recombinant technology used to produce it, was not new. That is, it was identical to natural erythropoietin. This was an unsurprising result for me given my research, but for the parties I suspect it was for neither had made that simple point to their Lordships during their two weeks of submissions (I attended the House of Lords as part of my PhD research and heard the entire appeal and made my own notes during the submissions).

The economic implications of the invalid Amgen patent over isolated erythropoietin and its manufacture have however never been assessed. It must be understood that a granted patent is a most powerful legal weapon. A patent provides the patent owner with the right to prevent anyone from using the technology that comes within its 20 year legal monopoly by seeking injunctions and with the right to damages or an account of profits for any infringement. Furthermore, in Australia such patented technologies are quarantined from laws that prohibit uncompetitive conduct, such as Part IV of the Trade Practices Act, 1974 (Cwth). As the law presently stands, no granted patent is guaranteed to be valid, yet there are no economic or legal consequences (other than the invalidity of a patent) that a patent owner must face if the patent that they own is subsequently held to be invalid by a Court. Although anyone can bring a patent revocation action in the courts the practical reality is that unless the challenging party is extremely wealthy and has substantial financial and legal resources recourse to this right is illusory. Most scientists, universities, laboratories, NGOs and interested individuals lack the necessary capacity

to sue to revoke a patent which they consider to be invalid. Those that do, namely multinational companies such as pharmaceutical and chemical companies, choose their battles very carefully.

This, of course brings me to the purpose of my post-doctoral research, which is to make it easier for scientists to carry out their research, but also to provide both Australian industry and science with an opportunity to avoid the potential disaster that will inevitably follow should investors in pharmaceutical, medical and biotechnological industries lose faith in the ability of the patent system (presently the only form of intellectual property available) to secure a financial return on their investment. The decision of the House of Lords in the above case is a warning that the patent system is not necessarily the answer. In this instance the impact of the decision on Amgen was negligible, but what if the decision was handed down ten years earlier?

Clearly, there is logic in the argument that patents help to encourage innovation, but the patent system has inherent limitations, one of which is that the subject of the patent must be an 'invention'. This requirement is acknowledged in Article 27.1 of *The Agreement on Trade-Related Aspects of Intellectual Property Rights* or TRIPS, one of the agreements that apply to all members of the World Trade Organisation (WTO). Arguably, patents that claim as inventions, isolated biological materials and their method of production fail to satisfy this requirement.

Now, we can either bury our heads in the sand and hope for the best, or we can acknowledge the problem and come to a solution that is fair and balanced and one that provides an incentive to investors but equally does not control scientists and researchers in their endeavours to innovate and overcome the causes of human disease and illness.

Australia is a member of the WTO and as such can instigate change to TRIPS so that a new intellectual property right can be developed.

In this regard my post doctoral research is directed to further developing what I call the Genetic Sequence Right or GSR.

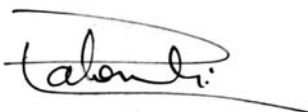
The GSR proposal recognises that the use of genetic sequences or biological materials (that are identical to naturally occurring sequences and materials) for whatever purpose should not be controlled nor come under the ownership and control of any one organisation or person. Its purpose is to encourage third party use, rather than attempting to control or restrict it. It recognises that irrespective of whether a genetic sequence is an 'invention' or not, the elucidation of a genetic sequence and the identification of its function is important work that should be encouraged. It therefore enables universities to fund their research projects by becoming GSR holders without incurring any obligation to pay GSR fees. It provides a system to record GSR's and assess the uses to which they are put. The fact that universities are in the business of education or, that today, see themselves as part of a broader commercial world becomes irrelevant.

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

I believe that it is the best interests of Australian science and industry and for the better health of all Australians that the Senate conduct a thorough Inquiry into the causes for the fall in innovation in Australian biotechnology and to provide an alternative form of intellectual property protection to the patent system.

I trust that my explanation in some four pages has adequately explained to you my concerns and the direction and purpose of my research. I would welcome the opportunity to elaborate and if there is any further information that I can provide you please do not hesitate to contact me.

Yours truly,



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