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To: [MDB-Patents-Consultation-Group](#)
Subject: Submission to consultation on proposed examination practice following the High Court decision in D'Arcy v Myriad Genetics Inc
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IP Australia consultation on proposed examination practice following the High Court decision in D'Arcy v Myriad Genetics Inc

Alphapharm welcomes the opportunity to comment on IP Australia's interpretation and proposed application of the High Court of Australia's decision in D'Arcy v Myriad Genetics Inc [2015] HCA 35. We are grateful for your consent to an extension till today to lodge our submission.

Alphapharm is Australia's leading supplier by volume of prescription medicines to the Pharmaceutical Benefits Scheme (PBS). One in seven prescriptions for PBS medicines is dispensed with an Alphapharm product. Our specialty is bringing patent-expired medicines to market, which contributes to the sustainability of the PBS by providing timely access to quality, safe, efficacious and affordable medicines. Alphapharm medicines, which have the same effect on the body as initial brands, are made to the highest global quality standards, including those of Australia's Therapeutic Goods Administration (TGA), the U.S. Food and Drug Administration, and the European Medicines Agency.

Alphapharm pioneered generic medicines in Australia in 1982 with twelve employees and four products. Today, we have 630 employees nationally, including 510 at our state-of-the-art manufacturing plant at Carole Park, Queensland. This year, the plant will produce 3 billion doses of medicine of which about 1.5 billion will be exported to some 50 countries around the world.

Alphapharm is part of Mylan, one of the world's leading global pharmaceutical companies. Mylan serves customers in more than 145 countries and territories. The company offers a growing portfolio of around 1,400 generic pharmaceuticals and several brand medications. The medicines range from difficult-to-manufacture dosage forms, such as injectables and transdermal patches, to HIV/AIDS antiretroviral (ARV) therapies, and include generic and brand-name products. The company has exceptional research and development capabilities and is one of the world's largest active pharmaceutical ingredient manufacturers. Mylan has a workforce of approximately 30,000.

Alphapharm has a copy of Dr Luigi Palombi's submission. We concur fully with it and adopt it for the purposes of this consultation.

Kind regards

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There are
7 billion
reasons
why we do what we do

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5 November 2015

A submission against IP Australia’s proposal to continue to permit the patenting of naturally occurring, isolated, purified or other kinds of biological materials except for nucleic acids, naturally occurring, isolated or synthesised including cDNA, that code for a polypeptide.

Summary: IP Australia’s interpretation and proposed application of the High Court of Australia’s decision in *D’Arcy v Myriad Genetics* [2015] HCA 35 (*Myriad*) is wrong. It proposes to continue to permit the patenting of naturally occurring, isolated, purified and other kinds of biological materials sourced from nature. In effect it means that ninety-eight percent of the human genome consisting of so-called ‘junk’ DNA, even when isolated from a human being, is patentable subject matter. This result is absurd, perverse and contrary to *Myriad*.

In *Myriad* the High Court unanimously rejected the rationale that IP Australia had employed for more than thirty years to justify the grant of patents claiming, as inventions, certain human genetic materials ‘isolated’ derived from natural environments, including synthetically produced complementary DNA (cDNA). The patent law principle that the High Court of Australia applied in *Myriad* is *not* confined to nucleic acids, naturally occurring, isolated or synthesised including cDNA, that code for a polypeptide.

Moreover, what IP Australia proposes is not only illegal¹ but improperly countermands the High Court of Australia.² Furthermore, it is a unilateral administrative decision that results in Australia contravening Art.27.1 of the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS).³ TRIPS mandates that patents be granted only in respect of “inventions”.⁴ Biological materials that are sourced from the natural environment, such as DNA, even when isolated, purified or synthesised, are not patentable subject matter -

¹ *Commissioner of Taxation v Indooroopilly Children Services (Qld) Pty Ltd* (2007) 158 FCR 325.

² “The primary or threshold requirement of a “patentable invention” is that it be an “invention”. The first step is to ask whether what is identified in the claim is an *invention*.” as per Gordon J, *D’Arcy v Myriad Genetics* at para 219.

³ Palombi, L (2003), ‘Patentable Subject Matter, TRIPS and the European Biotechnology Directive’, **26(3)**, *University of New South Wales Law Journal*, 782; Palombi, L (2004), *The Patenting of Biological Materials in the Context of TRIPS* (PhD Thesis: University of New South Wales, Australia; Luigi Palombi (2009), *Gene Cartels Biotech Patents in the Age of Free Trade*, (Edward Elgar, Cheltenham UK and Northampton, MA, USA).

⁴ Art 27.1 TRIPS: “ ... patents shall be made available for any *inventions* ...” (emphasis added)

they are not something that anyone invented. The same is true of other kinds of biological materials sourced from nature.

IP Australia’s misinterpretation and erroneous application of NRDC in regard to the patenting of biological materials.

For more than thirty years IP Australia has granted Australian patents containing claims to isolated biological materials sourced from nature. For more than thirty years IP Australia has justified the grant of such patents on its misinterpretation and erroneous application of the High Court of Australia’s decision in *National Research Development Corporation v The Commissioner of Patents* (1959) 102 CLR 252 (*NRDC*).

The truth of this assertion is unarguably demonstrated in various submissions made to the Australian Parliament by IP Australia and the Department of Innovation, Industry, Science and Research.

During the Senate Community Affairs Committee’s ‘Inquiry into Gene Patents’ conducted between 2009 and 2010, IP Australia and the Department of Innovation, Industry, Science and Research jointly submitted that:

“The courts have decided that patents can be granted for inventions that result in an ‘artificially created state of affairs’ in a ‘field of economic endeavour’. The courts have also recognised that the distinction between discoveries (which under patent law are considered not patentable) and inventions can be extremely fine. If ingenuity has been applied to a discovery to produce a new and useful result then it is an invention and may be patentable.

Australia’s current patents law does not give IP Australia any basis in law to refuse to patent genes, nucleic acid or protein sequences defined by their corresponding DNA sequence solely because the patent relates to these areas of technology. As such, IP Australia has granted patents over isolated and purified gene sequences, when other requirements for patentability under the Patents Act are met.”

During the Senate Legal and Constitutional Affairs Legislation Committee’s hearing into the ‘Patent Amendment (Human Genes and Biological Materials) Bill’ in between 2010 and 2011, once again in a joint submission, IP Australia and the Department of Innovation, Industry, Science and Research submitted:

“The key principle articulated in NRDC was that an invention is patentable if it gives rise to ‘an artificially created state of affairs’ in a ‘field of economic endeavour’. ... As noted previously, in Australia and most other countries, material which is isolated, purified or derived

from natural and living sources through human effort, is considered eligible for patent protection.”

In *Myriad* the High Court of Australia expressly and unanimously rejected the interpretation and application of *NRDC* as advocated in the above submissions.

French CJ and Kiefel, Bell and Keane JJ held:

“Counsel for Myriad posited "the test" in *NRDC* for patentability of a product as — "is it an artificially created state of affairs of economic utility? ". Myriad's approach was accepted by the primary judge who derived from *NRDC* the proposition that: "a product that consists of an artificially created state of affairs which has economic significance *will* constitute a 'manner of manufacture'." (emphasis added)

In similar vein, the Full Court said of *NRDC* that: "The Court held that it is sufficient for a product to result in 'an artificially created state of affairs', leading to 'an economically useful result'."

That proposition underpinned the conclusion by the Full Court in the second last paragraph of its judgment that:

"The isolated nucleic acid, including cDNA, has resulted in an artificially created state of affairs for economic benefit. The claimed product is properly the subject of letters patent. The claim is to an invention within the meaning of s 18(1) of the Act."

Myriad's proposition and the approach of the primary judge and the Full Court, with respect, rested *upon an unduly narrow characterisation* of the effect of the decision in *NRDC*. It rested upon the premise that the claims were for a product well within existing conceptions of a "manner of manufacture".” ...

Although it may be said in a formal sense that the invention as claimed, referring to isolated nucleic acids, embodies a product created by human action, that is not sufficient to support its characterisation as a manner of manufacture.” (emphasis added).

Gageler and Nettle JJ in referring to *NRDC* held:

“That holding is, however, to be understood as importing the Court's earlier observations as to the meaning of an "invention" and the idea that all that had come to be understood by that word, as used in patent law, is comprehended in the phrase "new manufactures". *It should not be taken to suggest that an "artificial state of affairs" and "economic utility" are the only considerations relevant to whether an invention is "a manner of manufacture" for the purposes of s 18(1)(a) of the Act.* (emphasis added) ...

Finally, much of the judgment at first instance and of the judgment of the Full Court appears to attribute *misplaced significance* to the conclusion reached in *NRDC* earlier set out that it was sufficient to render patentable the process or method of production there in suit that it had as its end result *an artificially created state of affairs of economic significance*. The judge at first instance concluded, and the Full Court appears to have taken a similar view, that: "It is apparent from this

passage that a product that consists of an artificially created state of affairs which has economic significance will constitute a 'manner of manufacture'."

With respect, that is not apparent and it is not the case." (emphasis added)

Gordon J held:

"... in the present appeal, the application of the passage from *NRDC* to claims 1-3 is inapposite. It is inapposite because applying or asking what the Full Court below saw as the questions posed in *NRDC* led to an *incorrect approach* to the construction of claims 1-3. The approach was *incorrect* because those questions necessarily required identification of an artificial state of affairs of some economic significance, *rather than directing attention to the more fundamental questions "what is the subject matter of the claim", "what is the invention" and "what are the facts and matters which are relied upon to justify a conclusion that the claim contains an invention?" ...*

To put it in functional terms, the fact that the isolated DNA has one or more of the characteristics of the code is *the function*. The fact that isolated nucleic acids cannot produce the natural polypeptide is irrelevant. Production of natural polypeptide is not a characteristic of claims 1-3.

To put it in structural terms, *the relevant structural attribute is that the product (the isolated DNA from a patient) contains an identical coding sequence to the coding sequence in the patient*. The fact that, as a consequence of isolation of the nucleic acid from the cell, other parts of the cell and the DNA are removed in that process is irrelevant." (emphasis added)

The High Court of Australia was critical of both the Federal and Full Federal Court decisions in *Myriad*, which it held wrongly sought to apply a rigid and formulaic 'test' of patentable subject matter. The High Court of Australia held:

"Myriad's proposition and the approach of the primary judge and the Full Court, with respect, rested upon an unduly narrow characterisation of the effect of the decision in *NRDC*. It rested upon the premise that the claims were for a product well within existing conceptions of a "manner of manufacture" This Court in *NRDC* *did not* prescribe a well-defined pathway for the development of the concept of "manner of manufacture" in its application to unimagined technologies with unimagined characteristics and implications." (emphasis added)

Moreover, the High Court of Australia criticised the failure of the Full Federal Court to take into account matters germane to public policy. The High Court of Australia held:

"The Full Court disclaimed any consideration of "whether, for policy or moral or social reasons, patents for gene sequences should be excluded from patentability." The question for its determination, however, was not whether a claimed invention, prima facie patentable,

should be denied patentability by judicial fiat. The question was whether the claimed invention lay within the established concept of a manner of manufacture and, if not, whether it should nevertheless be included in the class of patentable inventions as defined in s 18(1)(a) of the Act. Purposive and consequentialist considerations which, no doubt, could be classed as "policy" reasons may play a part in answering the second limb of that question.”

It is submitted, therefore, that IP Australia is, consistent with past erroneous practice, seeking to apply patent law, not as the High Court of Australia has ruled it is, but in accordance with what it believes patent law should be.

IP Australia’s misinterpretation and proposed erroneous application of *Myriad* in regard to the patenting of biological materials

The reasoning in *Myriad* is applicable to *any* biological material that is sourced from nature. IP Australia’s asserts that the High Court of Australia in *Myriad* “clearly concludes that a claim to an isolated nucleic acid that *merely represents information coding for a polypeptide* is not patent eligible” (emphasis added). While this statement is correct it is wrong, for the following reasons, to interpret and apply *Myriad* in the manner that IP Australia proposes.

First, the claims in contention are, as the High Court of Australia held, claims to a physical product. That product is a biological material. The biological material is DNA which, in terms of the patent in issue, is derived from the human genome, more specifically, from the human gene BRCA 1. The Court held that the biological materials defined by the claims in contention, not only contain “a [genetic] sequence that can properly be described as “information””⁵, but that “the information [is] stored in the sequence of nucleotides”.⁶ Nucleotides have a physical structure and perform a physical function which, relevantly, the Court acknowledged. The Court held that the claims defined a “product” that is “the medium in which that information resides.”⁷ Furthermore, in regard to that “product” the Court held that it contained “the same information as that contained in the DNA of the person from which the nucleic acid was isolated”.⁸ It is for this reason that the Court held: “the process of ‘isolation’ does not disclose a pathway to patentability.”⁹ In other words, the

⁵ Per French CJ, Kiefel, Bell and Keane JJ at para 89.

⁶ Ibid.

⁷ Ibid. (emphasis added)

⁸ Ibid.

⁹ Per French CJ, Kiefel, Bell and Keane JJ at para 86.

physical ‘isolation’ of naturally occurring biological materials from the natural environment from which they are sourced, not just the “nucleotides” defined by the claims in contention, involves a kind of human activity that does not distinguish such materials sufficiently to transform them from what they are into an ‘invention’¹⁰ within the meaning of the *Patents Act 1990*. The Court included “synthetic human DNA” known as complementary DNA or cDNA.

Secondly, while the Court’s analysis was directed to the claims in contention, as it had to be, the Court discussed the relevant science, which involved not only a consideration of that science with respect to protein-coding DNA, the biological material in issue, but to other biological materials, such as RNA, mRNA, histones, cells and their components, genes and proteins. The Court also considered the function of a gene (which contains both non-coding and protein-coding DNA) and its relationship to proteins and their production. And while the Court did so in the context of the human genetic code, the Court’s reasoning is equally applicable to non-human organisms. This is because DNA and the function it performs is not unique to humans. It is critical to cellular division. It is found in the cells of bacteria, viruses (although some viruses are RNA-only organisms), other microorganisms, plants, insects, reptiles, birds and mammals. Indeed, all organisms that have a capacity to replicate contain a genetic code that is unique to them at an individual level.

Thirdly, protein-coding DNA is merely one kind of DNA which, as it happens, is the subject of the claims in contention. That the Court was addressing claims to protein-coding DNA does not, with great respect, imply or suggest that the Court’s ruling in *Myriad* is confined to the subject matter of the claims in issue. Indeed, it is wrong to confine the Court’s ruling to DNA, protein coding or non-coding. The human genetic code, as the Court explained, is made up of nucleotides. Some nucleotides are protein-coding (about 2%), however, most are not (about 98%). Both kinds of DNA hold genetic information. It is now understood that non-coding DNA is not ‘junk’ DNA, as it was once believed and as IP Australia continues to call it. Both non-coding DNA and protein-coding DNA perform functions as well as having a physical shape and structure, which is not only critical to the performance of their respective functions, but ultimately to the integrity, reproducibility and viability of the organism with respect to which the genetic code is unique to.

¹⁰ *invention* means any manner of new manufacture the subject of letters patent and grant of privilege within section 6 of the Statute of Monopolies, and includes an alleged invention. Schedule to Patents Act 1990.

Fourthly, the Court’s ruling applies to other kinds of naturally occurring biological materials, whether ‘isolated’ or ‘purified’, such as proteins, bacteria and viruses, as well as “chemical molecules purified from natural sources”. The idea that the Court was only concerned with the informational characteristics of protein-coding DNA is a misreading of *Myriad*. The Court was considering the subject matter in the context that DNA is one form of naturally occurring biological material that has a physical structure and a natural function to perform. The fact that it is possible to extract from the human genome and use the extracted human protein-coding DNA to synthetically produce the identical protein in a purified form to that which the corresponding protein-coding DNA inside the human genome enables the human body to produce naturally, is immaterial. The protein, which is coded for also contains information in the form of an amino acid sequence. The amino acid sequence of the synthetic protein is identical to the amino acid sequence of the corresponding naturally produced protein. As the Court explained, the relationship between protein-coding DNA and the proteins that they code for is well known and understood. More to the point, that relationship owes nothing to the process of ‘isolation’ or ‘purification’. And the end result of that relationship is not merely information, it is a physical and tangible product. For example, the human protein, erythropoietin, has been synthetically produced. However, it has been held by a U.S. court in *Amgen, Inc v Chugai Pharmaceutical Co and Genetics Institute, Inc* (1989) 13 U.S.P.Q.2D 1737¹¹ to be identical in every way to the human produced erythropoietin:

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

¹¹ This case concerned what is known in U.S. patent law as an ‘interference’. The Court was required to determine which party was the first to invent under U.S. patent law. The issue of patentable subject matter was not before the Court and was not considered.

predicted by the equivalence of their immunological and biological activities.’”

Similarly, chemical molecules sourced from nature have, just like DNA molecules, physical structures. They are tangible products. And they also contain information. The information is not genetic information, rather it is chemical, but it is information nonetheless and, relevantly, it is information that owes nothing to the process of ‘isolation’ or ‘purification’. The chemical information describes the chemical composition and chemical constitution of naturally occurring chemical molecules. The purification step does not relevantly change naturally occurring chemical molecules, just as the isolation step, as held in *Myriad*, does not relevantly change naturally occurring DNAs.

There is a very relevant distinction to be made between “chemical molecules purified from natural sources” and a chemical molecule that is been produced by the use of organic chemistry. While both are in a pure form, their chemical formula and, therefore, their chemical composition and constitution are very different. For example, *acetylsalicylic acid*,¹² is an organic chemical molecule and is the active ingredient in the famous medicine known as ‘Aspirin’. *Acetylsalicylic acid* is a derivative of *salicin*,¹³ a chemical molecule extracted from plants such as White willow and meadowsweet. Both chemical molecules have the capacity to reduce pain and fever, but they are chemically different molecules.

The medicinal applications of *salicin* in managing pain and fever has been known for thousands of years, but the invention of *acetylsalicylic acid* in 1898 was made possible only with the advent of organic chemistry. *Acetylsalicylic acid* was, at the time of its invention, a new chemical entity. It was not naturally occurring. It was produced with the use of a new chemical process invented by Dr Felix Hoffmann. And it was this new chemical process that was *the* invention justifying the grant of a U.S. patent¹⁴ in 1900 to Farbenfabriken of Elberfeld Company (later Bayer). In order to gain a U.S. patent over *acetylsalicylic acid*, Dr Hoffmann described how his *process* was different and superior to the preexisting process developed by Dr Karl Kraut in 1869, and which yielded what he claimed was a ‘new compound’ - “the real acetyl salicylic acid”. *Acetylsalicylic acid* was at the time of its invention, a new chemical entity. Even so, the U.S. patent did not give Dr Hoffmann an patent over *acetylsalicylic acid* howsoever

¹² Chemical formula: C₉H₈O₄

¹³ Chemical formula: C₁₃H₁₈O₇

¹⁴ U.S. Patent 644,077 dated 27/2/1900.

made. The patent claim was to *acetylsalicylic acid* produced in accordance with his *inventive* chemical process.¹⁵

Therefore, “chemical molecules purified from natural sources” are not *new*. What may be new is the discovery that such chemical molecules may be useful in the development of medicines, such as antibiotics, but they themselves are not ‘new’. The first antibiotic medicine for the treatment of bacterial infection was developed in 1941. It became known as penicillin. Penicillin itself was not patented. What was patented in 1948 by the U.S. Department of Agriculture was a new process for the commercial production of penicillin.¹⁶ It is relevant to note that the ‘isolation’ of a naturally occurring biological material with antibiotic properties is only the *first* step in the development of an antibiotic medicine.¹⁷ The result of that ‘isolation’ *per se* is not a *new* chemical entity. And it is important to note that penicillin was ‘discovered’ by Prof Fleming in 1928, not invented. It was Profs Florey, Chain and Dr Heatley that proved the efficacy of his discovery for use in a new, albeit revolutionary, antibiotic medicine. It is not inappropriate to observe that Profs Fleming, Florey and Chain jointly shared the Nobel prize. This is self evident from the following description:

“The success of penicillin led to unparalleled efforts by government, academia and the pharmaceutical industry to *discover* other compounds from natural sources for the treatment of bacterial infections resulting in nearly all novel classes of antibiotics being from natural product sourced scaffolds through 1962. These were *discovered* simply by measuring zones of inhibition of bacterial strains on agar plates by applying whole broth or extracts obtained from microbial ferments.”¹⁸ (emphasis added)

Another important matter to note from the above history is the description of natural occurring antibiotic materials as “scaffolds” for the production of newer and more potent antibiotic medicines. The authors are making a relevant point of distinction between the naturally sourced antibiotic materials and their role in the development of antibiotic medicines. Accordingly, it is the case that these natural occurring antibiotic materials, even when isolated, are not the end product in the development of antibiotic medicines. They are merely the beginning.

¹⁵ See Attachment ‘A’.

¹⁶ U.S. Patent: 2,442,141 “Method for production of penicillin”.

¹⁷ Peláez, F. (2006) ‘The historical delivery of antibiotics from microbial natural products—Can history repeat?’, *Biomedical Pharmacology*, **71**(7), 981-990, 984.

¹⁸ Singh, F.B. and Barrett, J.F., (2006) ‘Empirical antibacterial drug discovery—Foundation in natural products’, *Biomedical Pharmacology*, **71**(7), 1006-1015, 1006.

The next step in the development of an antibiotic medicine using the ‘scaffold’ provided by the natural antibiotic material is ‘purification’. However, the act of invention in regard to this step is in the chemical process employed in its purification, because it is this step that enables the *concentration* of the isolated naturally occurring antibiotic material. This step is therefore important in the development of an antibiotic medicine. The inventive purification process developed by Profs Florey and Dr Chain (as he was at the time) was clearly at the forefront of the Nobel selection committee as is apparent from the presentation speech made at the award ceremony for Profs Fleming, Florey and Chain in 1945:

“The observation made by Professor Alexander Fleming which led to the *discovery* of penicillin, is now almost classical. ... In the purifying experiments then made [by Prof Florey and Dr Chain], the mould was cultivated in a special nutritive fluid in vessels, to which air could only gain access after it had been filtered through cotton wool. After about a week the penicillin content reached its highest value, and extraction followed. In this connection advantage was taken of the observation that the free penicillin is an acid which is more easily dissolved in certain organic solvents than in water, while its salts with alkali are more readily dissolved in water. The culture fluid was therefore shaken with acidified ether or amyl acetate. As, however, the penicillin was easily broken up in water solution, the operation was performed at a low temperature. Thus the penicillin could be returned to the water solution after the degree of acidity had been reduced to almost neutral reaction. In this way numerous impurities could be removed, and after the solution had been evaporated at a low temperature it was possible to obtain a stable dry preparation. The strength of this was up to 40-50 units per mg and it prevented the growth of staphylococci in a dilution of at least 1 per 1 million - thus the active substance had been successfully concentrated very considerably. It was therefore quite reasonable that it was thought that almost pure penicillin had been obtained - in a similar manner, in their work with strongly biologically active substances, many earlier researchers had thought that they were near to producing the pure substance.”

Relevantly, the chemical composition and structure of penicillin did not change. And as noted earlier, even when purified by this inventive chemical process, penicillin itself was not patented.

It is therefore important to note that the scope of the patent monopoly granted to Bayer for the substance that came to be known as ‘Aspirin’ was limited to the method of its synthesis even though its active ingredient, *acetylsalicylic acid*, was a *new* chemical entity in as much as it had a different chemical formula, composition and structure to the naturally occurring *salicin*, found in certain plants. Contrast this to penicillin which, even when purified by the use of an

inventive chemical process, is not chemically different in any way from naturally occurring penicillin. It is not a *new* chemical entity. Relevantly, penicillin was not patented. Clearly, the chemical process employed in its purification was patentable, however, at the time it was considered to be unethical in the United Kingdom and so Prof Florey and Dr Chain did not file a patent application over the purification process. That distinction eventually went to a U.S. government scientist, Dr Andrew Moyer, who developed a different process for the commercial production of penicillin. Dr Moyer's invention increased the yield of penicillin.¹⁹

Fifthly, IP Australia's assertion that isolated polyclonal antibodies, isolated polypeptides, synthesised polypeptides, isolated cells and isolated stem cells are patentable subject matter within the ruling of *Myriad* is also misguided. All of these biological materials are not relevantly changed by the process of isolation. Even their synthesis by human hands does not relevantly change their function or structure. As already explained, isolated and purified erythropoietin is identical in every way to naturally occurring erythropoietin. The same is true for non-human proteins such as receptors on the surfaces of viruses such as the hepatitis C virus.

Sixthly, even Australian patent attorneys do not accept IP Australia's misinterpretation of *Myriad*. According to the patent attorney firm Watermark, the Court's decision applies across the board, not just to protein-coding DNA. In a newsletter published by Watermark immediately after the Court's decision was handed down, the firm stated the following:

“The outcomes which have been observed in the United States since the Supreme Court *Myriad* Decision have confirmed our worst fears, with all isolated molecules, cells and other natural products being deemed to lack patent eligibility. That is, there was no basis upon which to confine the precedent created by this decision to nucleic acid molecules alone. There is little reason to believe that IP Australia, which will now have to consider how it instructs its examiners to apply this judicial decision, will not adopt a similar approach to the US Patent and Trademark Office, since the legal reasoning that the High Court has applied to dismissing the patentability of isolated DNA molecules *applies equally to all other isolated naturally occurring substances.*”²⁰

Finally, IP Australia has for decades employed erroneous legal reasoning to justify the grant of thousands of patents over naturally occurring biological materials. In 1991 IP Australia granted an Australian Patent No 624105 to Chiron Corporation entitled “Non-A

¹⁹ Moyer, A.J. and Coghil R.D., (1947) ‘The Effect of Phenylacetic Acid on Penicillin Production’, *Journal of Bacteriology*, 53(3): 329–341.

²⁰ Watermark Newsletter, ‘High Court rules *Myriad*'s BCRA genes not patentable subject matter in Australia’, per Dr Tania Obranovich, p.3.

Non B Hepatitis Diagnostics and Vaccines”. This patent contained thirty-nine claims. Included in these claims was a claim to hepatitis C virus nucleotides and polypeptides and to their use in diagnostics of any kind. The claims even included “purified HCV” and to an HCV vaccine. The patent claims, and the scope of the patent monopoly, were very broad. IP Australia granted this Australian patent even before the U.S. Patent Office did. Professor Baruch Blumberg, who discovered the hepatitis B virus and developed a vaccine to immunise against HBV infection, gave evidence in proceedings brought in the Federal Court of Australia challenging the validity of this patent. Unfortunately, the proceedings were settled during a nine week trial and the terms of that settlement remain confidential. However, during the course of the proceedings in 1994 Prof Blumberg, who was awarded the Nobel prize in Medicine in 1976 for his work on HBV, gave the following sworn testimony:

“I have reviewed Chiron's Australian Patent No. 624105 for the purposes of these proceedings. In my opinion, the claims in this patent are very broad. 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."* The issue can also be stated in scientific terms. This patent essentially does not distinguish between genotype and phenotype, whereas geneticists are very aware that such a distinction should be made. It is the reductionism argument taken to the extreme and it is not supported by the great weight of the history of scientific discovery in biology and medicine. To the extent that this extreme view is backed-up by broad claims, which it is in this patent, the effect will likely be inhibition of research on HCV.

Based on the unusually broad nature of the patent, if I were a research director for anti-virals and had the option of working on several viruses, the existence of this patent would weigh against my deciding to undertake HCV research. A company, or even an academic laboratory, might well be deterred from conducting research on HCV because the patent is, in effect, intimidating. With the patent as it stands, any investigator, particularly in commercial laboratories (where much of the work on hepatitis has been done) would have to seriously

consider that Chiron would bring an action against them if they attempted any commercialization of anything related to HCV.”

Beyond the one attempt by Murex Diagnostics in 1993 to challenge this patent, it went unchallenged for the twenty years permitted under Australian patent law. It is unsurprising that no HCV vaccine has been developed. Recently, more than thirty years after HCV was first patented, HCV anti-viral pharmaceuticals have become available in the United States. The cost of treatment is close to \$100,000. The cost has made it prohibitive for these medicines to be made available under the PBS. It is very likely that the patents granted to Chiron Corporation over HCV around the world, based on an erroneous policy applied by the U.S. Patent Office, IP Australia and other patent offices, permissive of the patenting of naturally occurring biological materials, has significantly hampered the development of an HCV vaccine and other medicines capable of treating HCV infection. And as the U.S. Supreme Court has recognised, too much patent protection can stifle innovation, rather than promote it.

Conclusion

As has been acknowledged by the U.S. Government and confirmed by the U.S. Supreme Court, the long standing policy once employed by the U.S. Patent and Trademark Office and permissive of the patenting of naturally occurring isolated and purified biological materials, such as isolated naturally occurring nucleic acids (nucleotides) and proteins (amino acids), is wrong and contrary to long established principles enshrined in U.S. patent law. This extends to synthetic constructs of isolated nucleic acids such as cDNA if the cDNA is *indistinguishable* from natural DNA. The U.S. Supreme Court did so in the context of various U.S. patents effectively corresponding to the patent in issue before the High Court of Australia in *Myriad*. There is no doubt, although the High Court did not expressly criticise IP Australia for adopting such a policy as did the U.S. Supreme Court of the USPTO, that as this submission overwhelmingly shows, it is wrong for IP Australia to interpret and apply *Myriad* by confining its reasoning only to protein-coding DNA. IP Australia must fully comply with the High Court of Australia’s ruling in *Myriad*. Its proposal does not. IP Australia fails to accept the error inherent in the policy behind its proposal, just as it failed to properly interpret and apply the High Court’s ruling in *NRDC* for more than thirty years.

UNITED STATES PATENT OFFICE.

FELIX HOFFMANN, OF ELBERFELD, GERMANY, ASSIGNOR TO THE FARBEN-FABRIKEN OF ELBERFELD COMPANY, OF NEW YORK.

ACETYL SALICYLIC ACID.

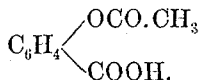
SPECIFICATION forming part of Letters Patent No. 644,077, dated February 27, 1900.

Application filed August 1, 1898. Serial No. 687,385. (Specimens.)

To all whom it may concern:

Be it known that I, FELIX HOFFMANN, doctor of philosophy, chemist, (assignor to the FARBENFABRIKEN OF ELBERFELD COMPANY, of New York,) residing at Elberfeld, Germany, have invented a new and useful Improvement in the Manufacture or Production of Acetyl Salicylic Acid; and I hereby declare the following to be a clear and exact description of my invention.

In the *Annalen der Chemie und Pharmacie*, Vol. 150, pages 11 and 12, Kraut has described that he obtained by the action of acetyl chlorid on salicylic acid a body which he thought to be acetyl salicylic acid. I have now found that on heating salicylic acid with acetic anhydride a body is obtained the properties of which are perfectly different from those of the body described by Kraut. According to my researches the body obtained by means of my new process is undoubtedly the real acetyl salicylic acid

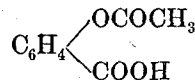


Therefore the compound described by Kraut cannot be the real acetyl salicylic acid, but is another compound. In the following I point out specifically the principal differences between my new compound and the body described by Kraut.

If the Kraut product is boiled even for a long while with water, (according to Kraut's statement,) acetic acid is not produced, while my new body when boiled with water is readily split up, acetic and salicylic acid being produced. The watery solution of the Kraut body shows the same behavior on the addition of a small quantity of ferric chlorid as a watery solution of salicylic acid when mixed with a small quantity of ferric chlorid—that is to say, it assumes a violet color. On the contrary, a watery solution of my new body when mixed with ferric chlorid does not assume a violet color. If a melted test portion of the Kraut body is allowed to cool, it begins to solidify (according to Kraut's statement) at from 118° to 118.5° centigrade, while a melted test portion of my product solidifies at about 70° centigrade. The melting-points of the two compounds cannot be compared, be-

cause Kraut does not give the melting-point of his compound. It follows from these details that the two compounds are absolutely different.

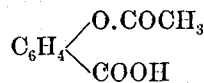
In producing my new compound I can proceed as follows, (without limiting myself to the particulars given:) A mixture prepared from fifty parts of salicylic acid and seventy-five parts of acetic anhydride is heated for about two hours at about 150° centigrade in a vessel provided with a reflux condenser. Thus a clear liquid is obtained, from which on cooling a crystalline mass is separated, which is the acetyl salicylic acid. It is freed from the acetic anhydride by pressing and then recrystallized from dry chloroform. The acid is thus obtained in the shape of glittering white needles melting at about 135° centigrade, which are easily soluble in benzene, alcohol, glacial acetic acid, and chloroform, but difficultly soluble in cold water. It has the formula



and exhibits therapeutical properties.

Having now described my invention and in what manner the same is to be performed, what I claim as new, and desire to secure by Letters Patent, is—

As a new article of manufacture the acetyl salicylic acid having the formula:



being when crystallized from dry chloroform in the shape of white glittering needles, easily soluble in benzene, alcohol and glacial acetic acid, difficultly soluble in cold water, being split by hot water into acetic acid and salicylic acid, melting at about 135° centigrade, substantially as hereinbefore described.

In testimony whereof I have signed my name in the presence of two subscribing witnesses.

FELIX HOFFMANN.

Witnesses:
R. E. JAHN,
OTTO KÖNIG.