[1996] UKHL 18

HOUSE OF LORDS

OPINIONS OF THE LORDS OF APPEAL FOR JUDGMENT IN THE CAUSE

BIOGEN INC. (APPELLANTS)

MEDEVA PLC (RESPONDENTS)

ON 31ST OCTOBER 1996

Lord Goff of Chieveley
Lord Browne-Wilkinson
Lord Mustill
Lord Slynn of Hadley
Lord Hoffmann

LORD GOFF OF CHIEVELEY

My Lords,

1. I have had the advantage of reading in draft the speech prepared by my noble and learned friend Lord Hoffmann. For the reasons he gives I would dismiss the appeal.

2. I wish to express the gratitude of the Appellate Committee to our two expert advisers, Professor D. Glover of the University of Dundee and Professor J. Neil of the University of Glasgow, who provided the Committee with invaluable assistance both before and during the hearing.

LORD BROWNE-WILKINSON

My Lords,

3. For the reasons given in the speech prepared by my noble and learned friend Lord Hoffmann I too would dismiss the appeal.

LORD MUSTILL

4. I have had the opportunity to read in draft the speech of my noble and learned friend Lord Hoffmann, and agree both with the conclusion that the appeal should be dismissed and with the reasons for that conclusion. In particular I am glad to adopt the proposed reconciliation of sections 14(5) and 72(1) of the Patents Act 1977, which eliminates a difficulty expressed by the Court of Appeal in *Genentech Inc.'s Patent* [1989] R.P.C. 147.

5. There is however one matter which I should mention: namely, the necessity or otherwise for a valid patent to concern an invention, as well as satisfying the conditions expressed in paragraphs (a) to *(b)* of Section 1(1) of the Act. This question was not contested before the House, although some reference was made to it in debate, for it was agreed (rightly in my opinion) that it has no bearing on the present appeal. My reason for referring to it is simply to make clear that in concurring with all your Lordships in the reasons for dismissing the appeal I should not be taken to accept, without full argument, that the need for an invention would always be academic, or that no such need is expressed by the words of section 1(1): nor indeed do I understand my noble and learned friend as advancing any conclusion to that effect. Certainly, in the great majority of cases, there will be no need to complicate the enquiry by looking outside the four conditions. The traditional law of patents is, however, in the course

of adapting itself to new technologies, beyond contemplation when the foundations of that law were established. This process is not without strain, and I believe that in some instances a close conceptual analysis of the nature of patentability will not be a waste of time. Such a case was *Genentech Inc.'s Patent* where the claim was for a product already existing in nature, a subject far distant from the mechanical and chemical inventions to which so much of traditional patent law relates. There may well be others in the future.

6. My Lords, my purpose in adding this footnote to the speech of my noble and learned friend is not of course to express any opinion, one way or the other, on the correctness of the reasoning outlined at pp. 261-266 of the report of *Genentech Inc.'s Patent.* The intention is only to emphasise that when a dispute does arise on which this question may have a bearing it will merit study leading to a definitive answer.

LORD SLYNN OF HADLEY

My Lords,

7. I have had the advantage of reading in draft the speech prepared by my noble and learned friend Lord Hoffmann. For the reasons he gives I too would dismiss the appeal.

LORD HOFFMANN

My Lords,

1. Genetic Engineering.

8. In this appeal your Lordships' House has for the first time to consider the validity of a patent for products of genetic engineering. This is a technology which has developed only during the last 25 years, in consequence of the great advances which have been made in our knowledge of the genetic code contained in every living cell. The code is embodied in a molecule of deoxyribonucleic acid ("DNA") which directs the cell to make the proteins which the organism requires. Genetic engineering or "recombinant DNA technology" consists of altering the DNA of a suitable cell so that it produces a protein which in nature occurs in another organism. In this way it has been possible to manufacture products of great medical importance which could not have been made by orthodox chemical synthesis.

2. The patent in suit.

9. The principal claim of the patent in suit is for an artificially constructed molecule of DNA carrying a genetic code which, when introduced into a suitable host cell, will cause that cell to make antigens of the virus hepatitis B ("HBV"). I shall have to describe in much greater detail what antigens are and how the invention enables them to be made. Suffice it for the moment to say that HBV is a widespread human virus, often causing fatal diseases of the liver, and that its antigens can be used both to test for whether someone has the virus and to make a vaccine which can give immunity against infection.

3. Biogen and Professor Murray.

10. The patent is based upon experimental work done in 1978 by Professor Sir Kenneth Murray of Edinburgh University. Recombinant DNA technology was then in its promising infancy. In February 1978 Professor Murray and a number of other molecular biologists of international repute, together with financial backers, met in Geneva and decided to found Biogen Inc, the patentee company ("Biogen"), for the purpose of exploiting the technology for commercial purposes. One of the first projects upon which they agreed was to try to make the antigens of HBV. Professor Murray began work in the spring of that year and in November reported that he had produced two of the known HBV antigens in colonies of cultured bacteria.

4. History of the proceedings and legal issues.

11. On 22 December 1978 Biogen filed a U.K. patent application describing what Professor Murray had done. This application, known in the proceedings as "Biogen 1" forms the basis of a claim to priority in respect of a later application filed with the European Patent Office ("EPO") in Munich on 21 December 1979. The European Patent was granted on 11 July 1990 and opposition proceedings were dismissed on appeal by the EPO on 28 July 1994.

12. Meanwhile, in 1992 Biogen began infringement proceedings against the respondent, Medeva plc, which was proposing to market what it described as a third-generation hepatitis B vaccine made by recombinant DNA technology in colonies of mammalian cells. Medeva counterclaimed for revocation. It alleged that the patent was invalid on a number of grounds. I shall briefly mention those which are still relied upon without at this stage making any comment or doing more than to refer to the sections of the Patents Act 1977 on which the objections are based. They are, first, that the claimed invention was obvious (sections l(l)(b) and 3), both at the date of application for the patent in suit and at the date of Biogen 1. Secondly, that Biogen was not entitled to the priority date of Biogen 1 because it did not "support" the invention claimed in the patent (section *5(2)(a)).* Thirdly, that the claimed invention was not an invention (section 1(1)), and fourthly, that the description in the specification was insufficient (section 72(l)(c)). Biogen concedes that the claimed invention was obvious at the date when the application for the European patent was filed but not that it was on the date of Biogen 1.

13. Aldous J. held that the claims in the patent were supported by the matter disclosed in Biogen 1 and that it was accordingly entitled to the earlier priority date. He dismissed all the objections and held the patent valid and infringed. The Court of Appeal (Nourse, Peter Gibson and Hobhouse L.JJ.) allowed an appeal. Hobhouse L.J. gave the judgment of the court. He held that Biogen 1 did not support the claimed invention and that in any case it was obvious at the earlier date. He would have been inclined, but for Medeva's counsel's lack of enthusiasm for the point, to hold that it was not an invention at all. He also held the description in the specification to be insufficient. From this comprehensive reverse Biogen appeals to your Lordships' House.

5. The state of the art in 1978.

14. In this appeal much turns upon identifying the inventive step, if any, in what Professor Murray did. There is no doubt that he was the first person to make HBV antigens by recombinant DNA technology. It does not however follow that he was inventive. The technology was developing very fast and recent developments might have made its use for that purpose obvious. Even if it was not, it does not follow that "making HBV antigens by recombinant DNA technology" would be the right way to describe his inventive step. Whenever anything inventive is done for the first time it is the result of the addition of a new idea to the existing stock of knowledge. Sometimes, it is the idea of using established techniques to do something which no one had previously thought of doing. In that case, the inventive idea will be doing the new thing. Sometimes, it is finding a way of doing something which people had wanted to do but could not think how. The inventive idea would be the way of achieving the goal. In yet other cases, many people may have a general idea of how they might achieve a goal but not know how to solve a particular problem which stands in their way. If someone devises a way of solving the problem, his inventive step will be that solution, but not the goal itself or the general method of achieving it. To discover precisely what constituted the inventive step, one must therefore examine the state of the art of molecular biology in 1978. Would it have been a new idea to think of making HBV antigens at all ? Or would that have been a goal which people had thought about but did not know how to achieve ? If the latter, would it have been inventive to think in general terms of using recombinant DNA technology ? Or would that also have been something which many molecular biologists would have wanted to do if only they could think of how to overcome particular difficulties which stood in their way ? To answer these questions, I must try to describe, as briefly as the nature of the subject will permit, what was the state of knowledge in December 1978, firstly, about the DNA of HBV, and, secondly, about the techniques of recombinant DNA technology. Both branches of

knowledge were then advancing at a considerable pace. It is not altogether easy to present a snapshot of the state of the art on the precise date when Biogen 1 was filed. As one would expect, some of the expert witnesses at the trial thought that the next steps were clear and obvious and others thought that they were difficult and doubtful. The judge made findings of fact on these questions to which I shall in due course return. For the moment, I can confine myself to matters which were not in dispute.

(a) HBV in 1978.

15. A paper published in 1970 by D.S. Dane and others ((1970) *Lancet,* i, 695-698) had made the suggestion, which by 1978 was generally accepted, that the infective agent of hepatitis B was a certain particle about 42 nanometres in diameter which had been found in the blood of infected people. ("Nano-" means one thousand millionth or 10^{-9}. A nanosecond is to a second what a second is to 30 years). The "Dane particle" appeared to include a circular molecule of DNA in a protein core and to be surrounded by a protein surface.

16. Proteins are complex molecules (their main elements are carbon, hydrogen, oxygen and nitrogen) formed from chains of amino acids linked to each other by peptide bonds (hence also known as "polypeptides") and folded into three-dimensional structures. There are twenty different amino acids and the order of amino acids in the chain will determine the geometric shape and chemical characteristics of the polypeptide.

17. The chemical structure of a viral protein may enable it to recognise a complementary structure on the surface of a suitable cell in its host organism, attach itself to that cell, introduce its own genetic material and thereby use the resources of the host cell to replicate itself. But similar processes of recognition may stimulate the immune system of the host organism to produce "antibodies," proteins which attach themselves to the virus and render it noninfectious. The proteins in the virus which cause the production of antibodies are called "antigens." An antibody recognises its corresponding antigen by a specific region of the latter's chemical structure known as its "epitope." The antibody will attach itself to the epitope which complements a region in its own molecular structure.

18. The relationship between antibody and antigen provides the means of both diagnosing and vaccinating against infection by the virus. If a patient has been infected with the virus, his blood will contain the corresponding antibodies. If the antigen can be purified or artificially made and introduced into a sample of the patient's blood, tests can show whether the blood contains any antibodies. This will indicate prior infection. A polypeptide which, by reason of having the right epitope, complements a particular antigen is said to display "antigen specificity" in respect of that antigen. Antigens can also be used for vaccination because once the immune system has been exposed to the antigen it will produce the relevant antibodies. Upon subsequent challenge by the antigen, it will produce the same antibodies much more quickly and copiously. A polypeptide which causes the immune system to produce an antibody is said to display "antigenicity." If a protein with the relevant antigenicity is introduced into the blood stream, it will put the immune system on alert. Thus the immune response will prevent or reduce the severity of infection on a subsequent exposure to the virus.

19. The Dane particle appeared to have at least two antigens, one at its core (hepatitis B core antigen or HBcAg) and one upon its surface (hepatitis B surface antigen or HBsAg). One way to obtain these antigens was to purify them from Dane particles taken from the blood of people infected by the virus. This had been done with some success. But there were concerns about the safety of such vaccines and supplies were limited by the number of donors. They could not be greatly enhanced by using infected laboratory animals because the virus infects only human beings and a few higher primates like chimpanzees.

20. Another theoretical possibility was to make the antigens artificially by orthodox chemical synthesis. But this required knowledge of the sequence and structure of the amino acids. In 1978, however, little was known about them. It appeared that there might be different strains of virus with surface antigens of different shapes. In April 1977 Darrell L. Peterson and others had published a paper *(Proc. Natl. Acad. Sci. USA* Vol. 74, pp. 1530-1534) in which they

described HBsAg as "a group of morphologically heterogenous, complex, macromolecular structures." They did identify a sequence of nine amino acids at the end of the polypeptide chain and ended by saying that complete information about the amino acid composition of HBsAg could achieve the goal of the synthetic vaccine.

21. A promising alternative method was recombinant DNA technology. For this purpose it was necessary to find the genes which coded for the antigens and insert these into a host cell which could express them in recoverable form. This involved two problems. The first was to find the genes. The most likely guess was that they were somewhere in the DNA of the Dane particle. But no one knew for certain. Secondly, there was much doubt about how one inserted them into a host cell and whether there was any available type of host cell in which they could be expressed. I shall enlarge upon these problems in the next section.

(b) Recombinant DNA technology in 1978.

22. Crick and Watson had discovered the structure of the DNA molecule in 1953. It consists of two strands of nucleic acid wound about each other in the form of a double helix. Each strand consists of a chain of nucleotides with a phosphate backbone. The nucleotides are distinguished only by their chemical bases, which consist of one of four chemicals: adenine (A), guanine (G), cytosine (C) and thymine (T). The bases in each strand are linked by hydrogen bonds to their complementary bases in the other strand, C pairing with G and T with A. The sequence of the bases in the nucleic acid strand constitutes a universal code, using four letters arranged in groups or "codons" of three, which determines the chemical processes in every living cell. A single complement of the DNA in an organism is called the "genome" and it includes, in complex organisms, many genes which code for the manufacture of different proteins.

23. The manufacture of a protein in a cell is preceded by a chemical reaction in which the two strands of DNA are separated. One strand is then copied or "transcribed" into a complementary sequence of bases in a single strand of nucleic acid called messenger ribonucleic acid ("mRNA"). By a series of complex chemical reactions, the sequence of bases is "translated" in its groups of three (or codons) into a defined sequence of amino-acids in a protein. Each of the 20 amino acids from which proteins are made is encoded by one or more codons. Thus the individual genes within the DNA, by the processes of transcription and translation, direct the synthesis of a sequence of amino acids which comprise a polypeptide. The reading process is initiated by a codon which constitutes a "start" or initiation signal and it is terminated, when the polypeptide is complete, by one of several codons which constitutes a "stop" or termination signal. The "start" sequence will also ensure that the protein synthesising machinery is in the right "reading frame," that is, that it reads each codon beginning with its first nucleotide rather than the second or third.

24. Recombinant DNA technology involves introducing a foreign DNA molecule, coding for a protein which is natural to a different organism, into a host cell in such a way that the artificially introduced gene is correctly transcribed and translated into the protein for which it codes. This requires coupling that DNA on to a "vector" DNA molecule so that the hybrid has the ability, first, to replicate within the host cell; secondly, to provide the correct signals to control transcription and translation; and thirdly, to provide a suitable marker function to enable host cells carrying the hybrid DNA molecule to be recognised. Two broad categories of DNA molecules will, on introduction into bacterial cells, either integrate themselves with the existing DNA of the cell or operate independently. In either case, they cause the cell to make the proteins encoded by their DNA. These are circular DNA molecules called plasmids and the DNA of viruses which infect bacteria ("bacteriophages" or "phages"). In the early 1970s techniques were developed whereby bacterial plasmid and bacteriophage DNA could be cut up and combined with fragments of DNA from other sources. It was therefore possible to take a sequence of foreign DNA which might encode a protein, introduce it into the DNA of a plasmid or phage and use the latter as a vehicle or "vector" to insert the DNA into a bacterial cell. In the late 1970s, these techniques were extended to permit the expression of foreign genes, but, just as it had previously been uncertain whether the foreign genes would survive in the bacteria, so there was uncertainty over the requirements for regulating expression.

25. Cutting up the DNA strands was achieved with the aid of enzymes called "restriction endonucleases." These digest specific sequences of nucleotides and therefore cut the DNA at a point called a "restriction site." The majority of restriction sites consist of four or six base sequences. For example, the enzyme called BamHI cuts DNA at the sequence GGATCC. As it happens, 1978 was the year in which the Nobel Prize was awarded to the discoverers of restriction endonucleases. When a strand of DNA has been cut with a restriction endonuclease, another fragment can be joined at that point with an enzyme called a DNA ligase. It is thus possible to "recombine" DNA from different sources to produce an artificial molecule.

26. By 1978 there were several ready-made vectors available which could be used to introduce chosen fragments of DNA into bacteria in order that they would replicate and provide large quantities of the foreign gene. One of the most popular was a recombinant plasmid known as pBR322 (its makers were Bolivar and Rodriguez). It was a circular molecule of DNA which had been put together from fragments of the DNA of several natural plasmids. It included restriction sites which enabled it to be cut at predetermined points with various enzymes. Although not widely used for expression studies, it contained suitable "start" and "stop" codes (called "expression control sequences") between which the foreign gene could be inserted. These expression control sequences regulate the expression of bacterial genes carried by the plasmid that serve as "markers;" genes which confer upon the host bacteria resistance to different antibiotics. This enabled one to test in the laboratory whether a bacterial cell had been "transformed" by the plasmid, that is, whether it had been taken up as part of the cell's genetic code, by seeing whether it survived contact with a given antibiotic. By 1978, a small number of experiments had shown that in certain cases foreign DNA could be expressed when the hybrid plasmid was introduced into the well-known bacterium called *Escherichia coli ("E. coli").*

27. Bacteria are extremely simple organisms classified as "prokaryotic" because they consist of single cells without nuclei. More complex ("eukaryotic") organisms have ceils with nuclear membranes. Until 1978 it was by no means clear that the protein-making equipment of a bacterial cell was up to the task of expressing the genes which coded for the proteins of eukaryotic cells. But that summer an important paper was published by Dr. Lydia Villa-Komaroff and others *(Proc. Natl. Acad. Sci. USA* Vol. 75, pp. 3727-3731). This proved conclusively that it was possible to express the DNA for the production of a eukaryotic cell protein (in that case, rat preproinsulin) by inserting it into pBR322 and transforming *E. coli.*

28. This discovery was highly relevant to the project for making the antigens of hepatitis B. Since the virus infects only higher organisms its proteins are necessarily eukaryotic. In 1978 vectors for transforming a eukaryotic host cell were still under development. The Biogen project for making the HBV antigens therefore required that they should be capable of being made in bacteria.

29. Professor Walter Gilbert of Harvard University, who had been the leader of the team doing the experiments which led to the Villa-Komaroff paper, was present at the Biogen founding meeting in Geneva. He was optimistic that any eukaryotic gene could be expressed in a foreign host. Others were more doubtful. The expression of rat preproinsulin had worked but there remained uncertainty about why it had worked. It did not follow that one could by similar means express all, or indeed any, other eukaryotic proteins.

30. Professor Murray also faced a difficulty which Dr Villa-Komaroff had been able to avoid. Eukaryotic DNA had been found to contain sequences of nucleotides which did not seem to code for anything. They were called "introns" or junk code. Eukaryotic cells had a mechanism for stripping out introns as part of the process of transcribing the DNA into mRNA. The mRNA which the cell's ribosomes translated into polypeptides was cleaned up and free of introns. However, no introns had been found in prokaryotic DNA. It was therefore assumed that prokaryotic organisms like *E. coli* had no mechanism for removing introns. This meant that the expression mechanism of a prokaryotic cell might be unable to cope with natural or "genomic" DNA coding for a eukaryotic protein and containing introns. A sequence of introns in the middle of the relevant gene could cause it to make the wrong amino acids, or shift the protein-

synthesising machinery into the wrong reading frame, or be read as a "stop" sequence and bring expression to a halt.

31. Dr Villa-Komaroff had been able to side-step this problem by using an artificial DNA ("cDNA") made by reverse transcription from natural mRNA which had been obtained from rats. This was an artificially cloned double copy of the mRNA from which the introns had already been removed. But Professor Murray had no source of mRNA from which he could make cDNA. All that he could obtain was genomic DNA from Dane particles.

32. One way to determine whether or not introns presented a problem would have been to "sequence" the HBV genome, that is, to identify the order of each base in the viral DNA molecule. It should then have been possible to discover where the relevant gene was and whether it contained introns or not. There was considerable uncertainty about the coding capacity of the viral DNA. There did not seem to be enough DNA, even without introns, to code for all the polypeptides which the virus contained. However, other explanations had been put forward. Some thought that the virus might use some of the host cell's DNA to encode some of the virion proteins. In 1978, however, the HBV genome had not yet been sequenced. A reliable technique for sequencing had been invented by Professor Gilbert, but it was laborious and slow. It was not until six months after the filing of Biogen 1 that the whole genome was sequenced by Valenzuela and others in the University of California at San Francisco *{Nature,* Vol. 280, 815-819). The genes which coded for the antigens were found to have no introns. It is because of this discovery and other advances in the state of the art that Biogen conceded that, by the date of its European filing, the method by which HBV antigens could be made was obvious. But the information was not available in 1978.

6. Biogen 1: Professor Murray's success.

33. I must now summarise what Biogen 1 discloses. Professor Murray purified some DNA from Dane particles and cut it into fragments with restriction enzymes chosen to digest the DNA at as few sites as possible. The object was to produce the largest possible fragments. There were two reasons for wanting large fragments. One was that screening large numbers of small fragments would be time-consuming. The other was to have the best chance of not cutting within the relevant gene, or, at any rate, within the part which coded for a relevant epitope. As Biogen 1 put it:

> "To be useful in the process a restriction enzyme should not cleave the HBV DNA within an essential part of the gene for antigenic specificity"

34. "Within an essential part of the gene" may mean that fragments of the antigenic polypeptide would do, provided that they displayed HBV antigen specificity. By the time of the EPO patent application, the claims make it clear that they cover not only the polypeptide but also fragments which exhibit the relevant properties. But Biogen 1 does not make anything of this point.

35. Professor Murray therefore chose the restriction enzymes Kpn I, Bg1II, Bam HI, Ava I and Eco RI all of which cut at six-nucleotide sites, these being mathematically less likely to occur than four-nucleotide sites.

36. Having obtained his large fragments, Professor Murray then employed established techniques of recombinant DNA technology to ligate the HBV DNA to pBR322 and introduce this into *E. coli.* In so doing, he followed almost exactly what Dr Villa-Komaroff had done to make rat prepro insulin. The antibiotic tests for ascertaining whether the bacterial cultures had been transformed by the plasmids and thus acquired antibiotic resistance were standard. The hybridisation tests which demonstrated that the colonies contained HBV DNA had been published in 1975. Professor Murray used a test for detecting antigen specificity which had been published by Broome and Gilbert earlier in 1978. Some of the cultures containing fragments cut with Kpn I and Bam HI tested positive. Biogen 1 does not say whether they

were positive for HBcAg or HBsAg but Professor Murray's evidence at the trial was that they were positive for both.

37. Biogen 1 describes the invention as based upon the discovery that HBV DNA, "when appropriately cleaved" and inserted into a vector such as a plasmid or phage, can be used to transform a micro-organism so that it produces polypeptides with HBV antigen specificity. It identifies as a "particularly surprising" feature of the invention the fact that genes from eukaryotic organisms "would not normally be expressed in bacteria."

38. Although, as I have said, Biogen 1 does not make separate reference to HBcAg and HBsAG, it plainly treats the invention as capable of being used to make both antigens. It says that depending upon the structure of the HBV DNA used and the means used to cleave it, the fragment may contain DNA which codes for one or more different antigens. It says that vectors other than pBR322 and host organisms other than *E. coli* (including yeasts or fungi) may be used. Finally it points out that known methods may be used to amplify production of the DNA and increase productivity of the host cells, thereby enabling large quantities of the antigens to be made.

7. *The claims of the patent in suit.*

39. I now set out the principal claims of the patent in suit, which Biogen 1 is said to support. Claim 1 reads as follows:

> 1. A recombinant DNA molecule characterized by a DNA sequence coding for a polypeptide or a fragment thereof displaying HBV antigen specificity, said DNA sequence being operatively linked to an expression control sequence in the recombinant DNA molecule and being expressed to produce a polypeptide displaying HBV antigen specificity when a suitable host cell transformed with said recombinant DNA molecule is cultured, the transformed host cell not producing any human serum proteins and any primate serum proteins other than the polypeptide displaying HBV antigen specificity.

40. The claim is to a product, a molecule identified partly by the way in which it has been made ("recombinant DNA") and partly by what it does (the words following "characterised by"). It generalises what Professor Murray had done in two ways. First, as to the results he had achieved. He had made a particular form of recombinant plasmid (pBR322 with fragments of Dane particle DNA) which had transformed *E. coli* and, he said, caused it to express the genes of HBcAg and HBsAg. The claim was for any recombinant DNA molecule which expressed the genes of any HBV antigen in any host cell. Secondly, there was generalisation of the method which he had used. He had made his DNA molecule from a standard pBR322 plasmid and large fragments from Dane particle DNA, chosen simply on the basis that they should be large. This was a technique imposed upon him by lack of information about the coding sequences. Thereafter, he employed conventional means to express the DNA in a conventional bacterial host. The claim was for any method of making a DNA molecule which would achieve the necessary expression.

41. Claims 2 to 4 are based upon claim 1:

> 2. The recombinant DNA molecule according to claim 1, characterized in that the polypeptide displaying HBV antigen specificity also displays HBV antigenicity.
>
> 3. The recombinant DNA molecule according to claim 1 or 2, characterized in that the DNA sequence codes for a polypeptide or a fragment thereof displaying the HBV antigen specificity of a hepatitis B virus core antigen.

> 4. The recombinant DNA molecule according to claim 1 or 2, characterized in that the DNA sequence codes for a polypeptide or a fragment thereof displaying the HBV antigen specificity of a hepatitis B virus surface antigen.

Claim 6 (as amended) is to:

> 6. A polypeptide free of any human serum proteins and any primate serum proteins which displays HBV antigen specificity, said polypeptide being produced by a host cell transformed with a recombinant DNA molecule according to claim 1 or 2.

Claims 7 and 8 are to polypeptides displaying respectively HBcAg and HBsAg specificity, produced by host cells transformed in accordance with claims 1, 2 or 3 or 1, 2 or 4 respectively.

8. Patentable Inventions.

42. Section 1(1) of the 1977 Act defines "patentable inventions." It says:

> 1(1) A patent may be granted only for an invention in respect of which the following conditions are satisfied, that is to say -
>
> *(a)* the invention is new;
>
> *(b)* it involves an inventive step;
>
> *(c)* it is capable of industrial application;
>
> *(d)* the grant of a patent for it is not excluded by subsections (2) and (3) below;
>
> and references in this Act to a patentable invention shall be construed accordingly.

9. What is an invention ?

43. The Act thus lays down various conditions, both positive (in paragraphs *(a)* to (c)) and negative (in paragraph *(d))* which an invention must satisfy in order to be a "patentable invention." This scheme might suggest that logically one should first decide whether the claimed invention can properly be described as an invention at all. Only if this question receives an affirmative answer would it be necessary to go on to consider whether the invention satisfies the prescribed conditions for being "patentable." In practice, however, I have no doubt that in most cases this would be a mistake and cause unnecessary difficulty.

44. The Act does not define the concept of an invention. Section 1(1) was intended to reflect, "as nearly as practicable," Article 52 of the European Patent Convention ("EPC"): see section 130(7) of the 1977 Act. Article 52 also has no definition of an invention. It seems that the parties to the EPC were unable to agree upon one: see Singer and Singer, *The European Patent Convention* (English edn. 1995 by Ralph Lunzer), para. 52.04). But the reason why the parties were content to do without a definition was that they recognised that the question would almost invariably be academic. The four conditions in section 1(1) do a great deal more than restrict the class of "inventions" which may be patented. They probably also contain every element of the concept of an invention in ordinary speech. I say probably, because in the absence of a definition one cannot say with certainty that one might not come across something which satisfied all the conditions but could not be described as an invention. But the draftsmen of the Convention and the Act, as well as counsel at the bar, were unable to think of any examples. Just in case one should appear, section 1(5) gives the Secretary of

State power to vary the list of matters excluded by paragraph (d) to "for the purpose of maintaining them in conformity with developments in science and technology."

45. As the four conditions are relatively familiar ground, elucidated by definitions in the Act and the jurisprudence of the courts and the EPO, it will normally be more convenient to start by deciding whether they are satisfied. In virtually every case this will be the end of the inquiry. There may one day be a case in which it is necessary to decide whether something which satisfies the conditions can be called an invention, but that question can wait until it arises.

46. One can of course imagine cases in which the alleged subject-matter is so obviously not an invention that it is tempting to take an axe to the problem by dismissing the claim without inquiring too closely into which of the conditions has not been satisfied. So in *Genentech Inc's Patent* [1989] R.P.C. 147, 264 Mustill L.J. said, by reference to the ordinary speech meaning of "invention":

> "You cannot invent water, although you certainly can invent ways in which it may be distilled or synthesised."

This is obviously right and in such a case it may seem pedantic to say that water fails the condition in paragraph *(a)* of section 1(1) because it is not new. Unfortunately, most cases which come before the courts are more difficult. Judges would therefore be well advised to put on one side their intuitive sense of what constitutes an invention until they have considered the questions of novelty, inventiveness and so forth. In the present case, I think that Medeva's counsel was right to resist the invitation of the Court of Appeal to make submissions on whether the claims constituted an invention.

10. Inventive Step

47. I will therefore first consider the question of whether what Professor Murray did in 1978 involved, as at the date of Biogen 1, an inventive step. Section 3 says:

> "An invention shall be taken to involve an inventive step if it is not obvious to a person skilled in the art, having regard to any matter which forms part of the state of the art by virtue only of section 2(2) above . . ."

Section 2(2) defines the state of the art:

> "The state of the art in the case of an invention shall be taken to comprise all matter (whether a product, a process, information about either or anything else) which has at any time before the priority date of that invention been made available to the public (whether in the United Kingdom or elsewhere) by written or oral description, by use or in any other way."

48. The question is therefore whether what Professor Murray did was obvious having regard to all matter which had been made available to the public before 22 December 1978. Aldous J., after hearing expert evidence about what people skilled in the art of recombinant DNA technology would have thought and done at the time, held that it was not. I will summarise his reasoning. He followed the procedure suggested by Oliver L.J. in *Windsurfing International Inc v. Tabur Marine (Great Britain) Ltd* [1985] R.P.C. 59, 73-74 by dividing the inquiry into four steps:

> "The first is to identify the inventive concept embodied in the patent in suit. Thereafter, the court has to assume the mantle of the normally skilled but unimaginative addressee in the art at the priority date and impute to him what was, at that date, common general knowledge in the art in question. The third step is to identify what, if any, differences exist between the matter cited as being "known or used" and the alleged invention. Finally, the court has to ask itself whether, viewed without any knowledge of the alleged invention, those

> differences constitute steps which would have been obvious to the skilled man or whether they require any degree of invention."

49. Aldous J. identified the inventive concept as "the idea or decision to express a polypeptide displaying HBV antigen specificity in a suitable host." The identification of the inventive concept is, as I have said, critical to this case and I shall have more to say about it later. At this stage I only observe that as formulated by Aldous J., the inventive concept means, in effect, having the idea of making HBV antigens by recombinant DNA technology. But that seems to me to be putting the matter far too wide. The idea of making HBV antigens by recombinant DNA technology was shared by everyone at the Geneva meeting of Biogen in February 1978 and no doubt by others working in the field, just as the idea of flying in an heavier-than-air machine had existed for centuries before the Wright brothers. The problem which required invention was to find a way of doing it.

50. Aldous J. then considered what would have been known to the man skilled in the art. I have already summarised what relevant information would have been available to the public in 1978. In particular, Aldous J. considered the importance of the Villa-Komaroff paper and said:

> "It is accepted that once a decision [had] been made to try expression of the HBV genome, the technique set out in Villa-Komaroff would have been sufficient to enable it to be carried out. Thus the difference between the prior art and the inventive concept is the idea or decision to express a polypeptide displaying HBV antigen specificity in a suitable host."

Again, I think that this is not a sufficiently specific way of stating the inventive concept. The general idea of expressing the gene for a polypeptide displaying HBV antigen specificity in a suitable host was, as I have said, fairly widely entertained. The inventive concept was the notion that Professor Murray's method of achieving the goal - creating large fragments of genomic DNA, ligating them to pBR322 and introducing the hybrid molecule into *E. coli* - would work.

51. Aldous J. then considered what strategies would have been available in 1978 to a skilled man who wanted to achieve the goal of making HBV antigens by recombinant DNA technology. One (strategy A) was to try to find out more about HBV and its DNA. In particular, one would sequence the genome. This would provide the information upon which a decision could be made as to whether and if so how to express the relevant genes. The alternative (strategy B) was, as Professor Murray had done, to take the genomic DNA and try to express it in *E. coli.* Biogen's case, as recorded by the judge, was that -

> "it was not until the sequence had been obtained, with the knowledge that introns would not be a problem, that the skilled man would seriously consider expression of HBV antigens."

The judge accepted this submission and held that Strategy B would not have been obvious in 1978. He said:

> "In the present case, there is no evidence to suggest that anyone, other than Biogen, contemplated expression of the HBV antigen in December 1978, despite the fact that the skilled man must have read the Villa-Komaroff paper and there was an incentive to do so. The reason may well be that stated in the patent, namely the skilled man was put off by introns."

He also rejected the argument that Strategy A was an obvious way of making the antigens. The evidence showed only that sequencing might show that there were no introns and that the gene could be expressed in bacteria but there was no ground for assuming that it would.

52. In the Court of Appeal, Hobhouse L.J. held that strategy B was obvious. The decision to adopt it was a "matter of business judgment," a "mere commercial decision." Biogen had made a

decision "to pursue an identified goal by known means." I think, with all respect to the closely-reasoned judgment of Hobhouse L.J., that the reference to a commercial decision is an irrelevancy. The fact that a given experimental strategy was adopted for commercial reasons, because the anticipated rewards seemed to justify the necessary expenditure, is no reason why that strategy should not involve an inventive step. An inventor need not pursue his experiments untouched by thoughts of gain. Most patents are the result of research programmes undertaken on the basis of hard-headed cost-benefit analysis. Nor do I think that the analogy of a bet is particularly helpful. In *Genentech Inc's Patent* [1989] R.P.C. 147, 281, Mustill L.J. said, in my opinion rightly, that "it cannot ... be assumed that inventiveness must have been involved somewhere, just because a wager on success could have been placed at long odds." The question is not what the odds were but whether there was an inventive step.

53. Having said this, I do think that Hobhouse L.J. was substantially correct in saying that Professor Murray had chosen to pursue an identified goal by known means. The goal of obtaining HBV antigens by recombinant DNA technology was obvious and the Villa-Komaroff method was by then part of the state of the art. If, therefore, the inventive concept was simply, as Aldous J. said, "the idea or decision to express a polypeptide displaying HBV antigen specificity in a suitable host," I would agree with Hobhouse L. J. that, so stated, the concept was obvious. It is however clear from the reasoning of Aldous J. that in order to explain why he regarded the decision as involving an inventive step it is necessary to describe it with rather more particularity. A proper statement of the inventive concept needs to include some express or implied reference to the problem which it required invention to overcome. The reasons why the expert witnesses thought it was not obvious to try the expression of genomic HBV DNA in *E. coli* were for the most part concerned with the uncertainties, in the absence of sequence information, about the presence of the HBV antigen genes in the Dane particle DNA, the perceived difficulties of expressing genomic eukaryotic DNA in a prokaryotic host, and, specifically, the problem of introns. It seems to me, therefore, that a more accurate way of stating the inventive concept as it appeared to Aldous J. is to say that it was the idea of trying to express unsequenced eukaryotic DNA in a prokaryotic host.

54. The question of whether an invention was obvious has been called "a kind of jury question" (see Jenkins L.J. in *Allmanna Svenska Elektriska A/B v. The Burntisland Shipbuilding Co. Ltd* (1952) 69 R.P.C. 63, 70) and should be treated with appropriate respect by an appellate court. It is true that in *Benmax* v. *Austin Motor Co. Ltd* [1955] A.C. 370 this House decided that, while the judge's findings of primary fact, particularly if founded upon an assessment of the credibility of witnesses, were virtually unassailable, an appellate court would be more ready to differ from the judge's evaluation of those facts by reference to some legal standard such as negligence or obviousness. In drawing this distinction, however, Viscount Simonds went on to observe, at p. 374, that it was "subject only to the weight which should, as a matter of course, be given to the opinion of the learned judge." The need for appellate caution in reversing the judge's evaluation of the facts is based upon much more solid grounds than professional courtesy. It is because specific findings of fact, even by the most meticulous judge, are inherently an incomplete statement of the impression which was made upon him by the primary evidence. His expressed findings are always surrounded by a penumbra of imprecision as to emphasis, relative weight, minor qualification and nuance *(as Renan said, la vérité est dans une nuance),* of which time and language do not permit exact expression, but which may play an important part in the judge's overall evaluation. It would in my view be wrong to treat *Benmax* as authorising or requiring an appellate court to undertake a *de novo* evaluation of the facts in all cases in which no question of the credibility of witnesses is involved. Where the application of a legal standard such as negligence or obviousness involves no question of principle but is simply a matter of degree, an appellate court should be very cautious in differing from the judge's evaluation.

55. In the present case I think that the reason why Hobhouse L.J. differed from the judge on the question of obviousness was not because of any failure to give sufficient weight to the judge's evaluation of the evidence but because he took at face value the judge's statement of the inventive concept. On the other hand, if the concept is reformulated in accordance with the judge's reasoning as I have suggested, the argument for the existence of an inventive step is much stronger. If no question of principle were involved, I think it would be wrong to interfere with the judge's assessment. But the inventiveness alleged in this case is of a very unusual

kind. It is said to consist in attempting something which a man less skilled in the art might have regarded as obvious, but which the expert would have thought so beset by obstacles as not to be worth trying. In *The Raleigh Cycle Co. v. H. Miller & Co.* (1946) 63 R.P.C. 113 the Court of Appeal was prepared to assume that it could be inventive to realise that a bicycle hub dynamo of conventional design could function satisfactorily even though it rotated at a lower speed than was previously thought essential. There may be a question of principle here but, like the Court of Appeal in that case, I shall not pursue the question of whether this amounts to an inventive step for the purposes of patent law because I am content to assume, without deciding, that what Professor Murray did was not obvious.

11. Priority date

56. The next question is whether, given that Biogen 1 disclosed what would at the time have been a patentable invention, it "supports" the invention actually claimed in the patent in suit. This question must be answered in the affirmative if Biogen is to be able to rely on the date of Biogen 1 as its priority date in accordance with section 5(2)(a). The relevant provisions are as follows:

> 5(1) For the purposes of this Act the priority date of an invention to which an application for a patent relates and also of any matter (whether or not the same as the invention) contained in any such application is, except as provided by the following provisions of this Act, the date of filing the application.
>
> (2) If in or in connection with an application for a patent (the application in suit) a declaration is made, whether by the applicant or any predecessor in title of his, complying with the relevant requirements of rules and specifying one or more earlier relevant applications for the purposes of this section made by the applicant or a predecessor in title of his and each having a date of filing during the period of twelve months immediately preceding the date of filing the application in suit, then -
>
> > *(a)* if an invention to which the application in suit relates is supported by matter disclosed in the earlier relevant application or applications, the priority date of that invention shall instead of being the date of filing the application in suit be the date of filing the relevant application in which that matter was disclosed or, if it was disclosed in more than one relevant application, the earliest of them;

57. In *Asahi Kasei Kogyo KK's Application* [1991] R.P.C. 485 this House decided that for matter to be capable of supporting an invention within the meaning of section *5(2)(a)* it must contain an "enabling disclosure," that is to say, it must disclose the invention in a way which will enable it to be performed by a person skilled in the art. This construction has not been challenged by the appellants before your Lordships' House. It is however important to notice the relationship between the requirement of "support" in section 5(2)(a) and certain other provisions of the Act which share the concept of an enabling disclosure.

58. The concept of an enabling disclosure is central to the law of patents. For present purposes, it touches the matters in issue at three different points. First, as we have seen, it forms part of the requirement of "support" in section *5(2)(a).* Secondly, it is one of the requirements of a valid application in section 14. And thirdly, it is essential to one of the grounds for the revocation of a patent in section 72. I shall start with section 14. Subsection (3) says:

> "The specification of an application shall disclose the invention in a manner which is clear enough and complete enough for the invention to be performed by a person skilled in the art."

This is plainly a requirement of an "enabling disclosure." In addition, subsection *(5)(c)* says that the claim or claims shall be "supported by the description." It was by reference to subsection (3) that Lord Oliver of Aylmerton, who gave the leading speech in *Asahi,* reasoned, at p. 536 that a description would not "support" the claims for the purpose of subsection (5)(c) unless it contained sufficient material to enable the specification to constitute the enabling disclosure which subsection (3) required: "the Act can hardly have contemplated a complete application for a patent lacking some of the material necessary to sustain the claims made." By parity of reasoning, he said that "support" must have the same meaning in section 5(2)(a).

59. The absence of an enabling disclosure is likewise one of the grounds for the revocation of a patent specified in section 72(1). Paragraph *(c)* says that one such ground is that -

> "the specification of the patent does not disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art."

This is entirely in accordance with what one would expect. The requirement of an enabling disclosure in a patent application is a matter of substance and not form. Its absence should therefore be a ground not only for refusal of the application but also for revocation of the patent after grant. Similarly, the same concept is involved in the question of whether the patent is entitled to priority from an earlier application. This is not to say that the question in each case is the same. The purposes for which the question is being asked are different. But the underlying concept is the same.

60. The explanation of section 14(5)(c) in *Asahi* seems to me to provide an answer to a point which puzzled the Court of Appeal in *Genentech Inc's Patent* [1989] R.P.C. 147. The court noted that although section 14(5)(c) is a statutory requirement for a valid patent application, non-compliance is not a ground for revocation of a patent which has been granted. Section 72(1) states exhaustively the grounds upon which a patent may be revoked. These grounds do not, as such, include non-compliance with section 14(5). But the substantive effect of section 14(5)(c), namely that the description should, together with the rest of the specification, constitute an enabling disclosure, is given effect by section 72(1)(c). There is accordingly no gap or illogicality in the scheme of the Act.

61. The need for an enabling disclosure to satisfy the requirements of support under section *5(2)(a),* valid application under section 14 and sufficiency under section 72(1*)(c)* has, I think, been plain and undisputed since the decision in *Asahi.* What has been less clear is what the concept of an enabling disclosure means. Part of the difficulty has been caused by a misinterpretation of what the Technical Board of Appeal of the EPO said in *Genentech I/Polypeptide expression* (T 292/85) [1989] OJEPO 275. This was a patent for an plasmid suitable for transforming a bacterial host which included an expression control sequence or "regulon" which could enable the expression of foreign DNA as a recoverable polypeptide. The Examining Division was willing to grant a patent only in respect of the plasmids, bacteria and polypeptides known at the date of application. The Technical Board of Appeal allowed the appeal, saying that the Examining Division had taken too narrow a view of the requirement of enabling disclosure:

> "What is also important in the present case is the irrelevancy of the particular choice of a variant within the functional terms 'bacteria,' 'regulon' or 'plasmid.' It is not just that <u>some</u> result within the range of polypeptides is obtained in each case but it is the <u>same</u> polypeptide which is expressed, independent of the choice of these means. . . . Unless variants of components are also embraced in the claims, which are, now or later on, equally suitable to achieve the same effect in a manner which could not have been envisaged without the invention, the protection provided by the patent would be ineffectual . . . The character of the invention this time is one of general methodology which is fully applicable with any starting material, and is, as it was already stated, also independent from the known, trivial, or inventive character of the end-products."

In other words, the applicants had invented a general principle for enabling plasmids to control the expression of polypeptides in bacteria and there was no reason to believe that it would not work equally well with any plasmid, bacterium or polypeptide. The patent was therefore granted in general terms.

62. In *Molnlycke AB* v. *Procter & Gamble Ltd* [1992] FSR 549, however, Morritt J. interpreted this decision to mean that it was a general rule of European patent law that an invention was sufficiently disclosed if the skilled man could make a single embodiment. This interpretation was followed by Aldous J. in *Chiron Corporation v. Organon Teknika Ltd* [1994] FSR 202, although I think I detect in his judgment some surprise that the EPO should have adopted such a mechanistic and impoverished approach to the concept of enabling disclosure. As we shall see, he applied the same rule in the present case.

63. In fact the Board in *Genentech I/Polypeptide expression* was doing no more than apply a principle of patent law which has long been established in the United Kingdom, namely, that the specification must enable the invention to be performed to the full extent of the monopoly claimed. If the invention discloses a principle capable of general application, the claims may be in correspondingly general terms. The patentee need not show that he has proved its application in every individual instance. On the other hand, if the claims include a number of discrete methods or products, the patentee must enable the invention to be performed in respect of each of them.

64. Thus if the patentee has hit upon a new product which has a beneficial effect but cannot demonstrate that there is a common principle by which that effect will be shared by other products of the same class, he will be entitled to a patent for that product but not for the class, even though some may subsequently turn out to have the same beneficial effect: see *May & Baker Ltd* v. *Boots Pure Drug Co Ltd* (1950) 67 R.P.C. 23, 50. On the other hand, if he has disclosed a beneficial property which is common to the class, he will be entitled to a patent for all products of that class (assuming them to be new) even though he has not himself made more than one or two of them.

65. Since *Genentech I/Polypeptide expression* the EPO has several times reasserted the well established principles for what amounts to sufficiency of disclosure. In particular, in *Exxon/Fuel Oils* (T 409/91) [1994] OJEPO 653, para. 3.3., the Technical Board of Appeal said of the provision in the European Patent Convention equivalent to section 14(5)(c) of the Act:

> "Furthermore, Article 84 EPC also requires that the claims must be supported by the description, in other words, it is the definition of the invention in the claims that needs support. In the Board's judgment, this requirement reflects the general legal principle that the extent of the patent monopoly, as defined by the claims, should correspond to the technical contribution to the art in order for it to be supported, or justified."

12. Support for the claims

66. I come therefore to the question of whether Biogen 1 contained an enabling disclosure which supported the claims in the patent in suit. The argument before Aldous J. seems to have concentrated on the questions of whether it had been shown that Professor Murray's method was capable of making both HBcAg and HBsAg and whether it would work in eukaryotic as well as bacterial hosts. The judge, following his earlier decision in *Chiron Corporation* v. *Organon Teknika Ltd* [1994] FSR 202, said that it would be enough if the specification enabled one embodiment to be made. As there was no doubt that Professor Murray had made HBcAg in cultures of *E. coli,* that was an end of the matter. In case it was considered that the claims really amounted to two inventions, one for making HBcAg and another for HBsAg, he found that the skilled man would also have been able to make HBsAg. Having heard the evidence of Professor Murray and others, he said:

> "Upon the evidence, I conclude that Biogen did express and demonstrate expression of the surface antigen using the techniques described in the specification."

The disclosure was therefore sufficient in respect of both inventions.

67. In the opposition proceedings in the EPO, the argument proceeded upon similar lines. The only issue on sufficiency seems to have been whether the invention could produce HBsAg as well as HBcAg. The Technical Board, like Aldous J., found as a fact that it could. The question of whether the method could be used in other hosts was not argued, the opponents thinking (probably rightly) that this point was concluded against them by the EPO decision in *Genentech I/Polypeptide expression.* In fact, if Professor Murray's method worked in a prokaryotic host, despite the possibility that such a host might not be able to cope with introns, it was even more likely to work in a eukaryotic host, which was better equipped for dealing with them. For my part, therefore, I would not differ from the findings of either Aldous J. or the Technical Board in rejecting both these grounds of opposition.

68. In the Court of Appeal, Hobhouse L.J. began his judgment by saying that he did not believe that the court was differing from Aldous J. "on any question of the acceptance of the evidence of witnesses or primary scientific fact." He nevertheless made a thorough re-examination of the evidence on whether the method disclosed in Biogen 1 had enabled the making of HBsAg and came to the conclusion that it had not. He said:

> "The outcome of this evidence is that whatever results the plaintiff obtained in 1978 did not amount to evidence justifying a claim to have produced a recombinant DNA molecule which enabled the expression of HBsAg in *E. coli* (or any other host)."

69. I am bound to say that I regret the decision of the Court of Appeal to revisit the evidence upon which the judge made his finding of fact. For the reasons given earlier in relation to the issue of obviousness, I think that this was a question on which greater respect should have been paid to the judge's findings. The Court of Appeal's reversal of the judge on this issue greatly lengthened the hearing before your Lordships' House, as no doubt it had done in the Court of Appeal. The House was invited to undertake a minute examination of the facts with a view to restoring the findings of the judge. It was even offered inspection of the autoradiographs claimed to show the positive results upon which Professor Murray had based his claim to success -an offer which your Lordships felt able to decline. But I think that your Lordships learned enough of the detailed facts to form the view that the judge's decision was one which was open to him upon the evidence and should not have been disturbed.

70. But the fact that the skilled man following the teaching of Biogen 1 would have been able to make HBcAg and HBsAg in bacterial cells, or indeed in any cells, does not conclude the matter. I think that in concentrating upon the question of whether Professor Murray's invention could, so to speak, deliver the goods across the full width of the patent or priority document, the courts and the EPO allowed their attention to be diverted from what seems to me in this particular case the critical issue. It is not whether the claimed invention could deliver the goods, but whether the claims cover other ways in which they might be delivered: ways which owe nothing to the teaching of the patent or any principle which it disclosed.

71. It will be remembered that in *Genentech I/Polypeptide expression* the Technical Board spoke of the need for the patent to give protection against other ways of achieving the same effect "in a manner which could not have been envisaged without the invention." This shows that there is more than one way in which the breadth of a claim may exceed the technical contribution to the art embodied in the invention. The patent may claim results which it does not enable, such as making a wide class of products when it enables only one of those products and discloses no principle which would enable others to be made. Or it may claim every way of achieving a result when it enables only one way and it is possible to envisage other ways of achieving that result which make no use of the invention.

72. One example of an excessive claim of the latter kind is the famous case of *O'Reilly* v. *Morse* (1854) 56 U.S. (15 How.) 62 in the Supreme Court of the United States. Samuel Morse was the first person to discover a practical method of electric telegraphy and took out a patent in which he claimed any use of electricity for "making or printing intelligible characters, signs, or letter, at any distances." The Supreme Court rejected the claim as too broad. Professor Chisum, in his book on Patents (vol. 1, § 1.03[2] summarises the decision as follows:

> "Before Morse's invention, the scientific community saw the possibility of achieving communication by the 'galvanic' current but did not know any means of achieving that result. Morse discovered one means and attempted to claim all others."

73. A similar English case is *British United Shoe Machinery Co Ltd* v. *Simon Collier Ltd* (1908) 26 R.P.C. 21. The patentee invented a piece of machinery for automatically trimming the soles of boots and shoes by means of a cam. One of the claims was in general terms for automatic means of trimming soles. Parker J. said, at pp. 49-50:

> "... [T]he problem was simply how to do automatically what could already be done by the skill of the workman. On the other hand, the principle which the inventor applies for the solution of the problem is the capacity of a cam to vary the relative positions of two parts of a machine while the machine is running. Assuming this principle to be new, it might be possible for the inventor, having shown one method of applying it to the solution of the problem, to protect himself during the life of his Patent from any other method of applying it for the *same* purpose, but I do not think that the novelty of the principle applied would enable him to make a valid claim for all means of solving the problem whether the same or a different principle were applied to *its* solution."

74. I return therefore to consider the technical contribution to the art which Professor Murray made in 1978 and disclosed in Biogen 1. As it seems to me, *it* consisted in showing that despite the uncertainties which then existed over the DNA of the Dane particle - in particular, whether it included the antigen genes and whether it had introns - known recombinant techniques could nevertheless be used to make the antigens in a prokaryotic host cell. As I have said, I accept the judge's findings that the method was shown to be capable of making both antigens and I am willing to accept that it would work in any otherwise suitable host cell. Does this contribution justify a claim to a monopoly of *any* recombinant method of making the antigens? In my view it does not. The claimed invention is too broad. Its excessive breadth is due, not to the inability of the teaching to produce all the promised results, but to the fact that the same results could be produced by different means. Professor Murray had won a brilliant Napoleonic victory in cutting through the uncertainties which existed in his day to achieve the desired result. But his success did not in my view establish any new principle which his successors had to follow if they were to achieve the same results. The inventive step, as I have said, was the idea of trying to express unsequenced eukaryotic DNA in a prokaryotic host. Biogen 1 discloses that the way to do it is to choose the restriction enzymes likely to cleave the Dane particle DNA into the largest fragments. This, if anything, was the original element in what Professor Murray did. But once the DNA had been sequenced, no one would choose restriction enzymes on this basis. They would choose those which digested the sites closest to the relevant gene or the part of the gene which expressed an antigenic fragment of the polypeptide. The metaphor used by one of the witnesses was that before the genome had been sequenced everyone was working in the dark. Professor Murray invented a way of working with the genome in the dark. But he did not switch on the light and once the light was on his method was no longer needed. Nor, once they could use vectors for mammalian cells, would they be concerned with the same problem of introns which had so exercised those skilled in the art in 1978. Of course there might be other problems, but Biogen 1 did not teach how to solve them. The respondents Medeva, who use restriction enzymes based on knowledge of the HBV genome and mammalian host cells, owe nothing to Professor Murray's invention.

75. It is said that what Professor Murray showed by his invention was that it could be done. HBV antigens could be produced by expressing Dane particle DNA in a host cell. Those who followed, even by different routes, could have greater confidence by reason of his success. I do not think that this is enough to justify a monopoly of the whole field. I suppose it could be said that Samuel Morse had shown that electric telegraphy could be done. The Wright Brothers showed that heavier-than-air flight was possible, but that did not entitle them to a monopoly of heavier-than-air flying machines. It is inevitable in a young science, like electricity in the early nineteenth century or flying at the turn of the last century or recombinant DNA technology in the 1970s, that dramatically new things will be done for the first time. The technical contribution made in such cases deserves to be recognised. But care is needed not to stifle further research and healthy competition by allowing the first person who has found a way of achieving an obviously desirable goal to monopolise every other way of doing so. (See Merges and Nelson, *On the Complex Economics of Patent Scope* (1990) 90 Columbia Law Review 839.)

76. I would therefore hold that Biogen 1 did not support the invention as claimed in the European Patent and that it is therefore not entitled to the priority date of Biogen 1. As it is conceded that the invention was obvious when the patent application was filed, it is invalid.

13. The EPO decision.

77. I must at this point say something about the decision of the Technical Board of the EPO, which dismissed opposition proceedings and held the patent valid. Decisions of the EPO on questions of law are, as this House said in *Merrell Dow Pharmaceuticals Inc* v. *H.N. Norton & Co. Ltd* [1996] R.P.C. 76, 82, of considerable persuasive authority. But the decision of the EPO in this case did not, as it seems to me, proceed on any principle different from those I have endeavoured to apply. The Board held, as I have been willing to assume, that the invention described in Biogen 1 was not obvious at the priority date. On the other hand it held that the disclosure in Biogen 1 was in respect of the same invention as that claimed in the patent and, contrary to my view hereafter expressed, that such disclosure was sufficient to enable the invention to be performed to the full extent of the claims. But in arriving at this conclusion, the Board directed its attention solely to the question of whether the teaching in Biogen 1 would enable the man skilled in the art to achieve expression of HBsAg as well as HBcAg. Nothing was said about whether the claims were too broad because expression could also be achieved without the use of the teaching which it contained, by a method of which it could not be said, in the words of the Technical Board in *Genentech I*, that it was "in a manner which could not have been envisaged without the invention." But the principle upon which I have come to the conclusion that on this ground the patent is invalid is also, as I have said, clearly stated in decisions of the EPO such as *Genentech I* and *Exxon.* I would not therefore regard the outcome of this appeal as suggesting any divergence between the jurisprudence of this court and that of the EPO.

14. Sufficiency

78. If your Lordships are agreed that, lacking the support of an earlier priority date, the patent is invalid for obviousness, it is unnecessary to consider whether it was also invalid for insufficiency and therefore liable to be revoked under section 72(1)(c). But the reasoning by which I have come to the conclusion that the patent was not entitled to the earlier priority also, in my view, leads to the conclusion that it was insufficient. I should however mention one point of some general importance concerning the construction of this provision which arose in the course of argument. This is the question of the date on which the specification must "disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art." The Court of Appeal thought it was the date of filing of the application, which in this case was 21 December 1979. Aldous J. said it was the date upon which the application was published, which was 28 May 1986. On the latter view, a specification may be insufficient when the application is filed but satisfy section 72(1*)(c)* because of advances in the art made between then and the date of publication. I do not think that the point arises in this case, because, whatever date one chooses, the patent did not disclose any method for making the antigens other than that disclosed in Biogen 1. It therefore remained insufficient for the

purpose of sustaining a claim to every recombinant DNA method. Nevertheless, since the point was argued and there was a difference of view in the courts below, I shall shortly express my own opinion.

79. Aldous J. followed a number of authorities which held that the date of publication was the date for deciding the question of sufficiency under the Patents Act 1949. The reasoning was that the purpose of requiring a specification was to allow the public to work the invention after the expiry of the monopoly. This in itself might suggest that it was enough if the disclosure was sufficient when the patent expired. But, as Buckley L.J. said in *Standard Brands Inc.'s Patent (No. 2)* [1981] R.P.C. 499, 529, the public was also entitled to know as soon as the patent is published whether it was valid or not. This pointed to the date of publication. He also drew attention to the fact that the specification might have been amended after filing. Such amendments would be treated as relating back to the date of filing and it would therefore be inappropriate to test sufficiency by reference to the specification originally filed.

80. In my view, however, there is an important difference between the 1949 and 1977 Acts which make decisions on the earlier Act an unsafe guide. Section 72(1)(c) of the 1977 is not only intended to ensure that the public can work the invention after expiration of the monopoly. It is also intended to give the court in revocation proceedings a jurisdiction which mirrors that of the Patent Office under section 14(3) or the EPO under Article 83 of the EPC, namely, to hold a patent invalid on the substantive ground that, as the EPO said in *Exxon/Fuel Oils* (T 409/91) [1994] OJEPO 653, para. 3.3., the extent of the monopoly claimed exceeds the technical contribution to the art made by the invention as described in the specification. In the 1949 Act, this function was performed by another ground for revocation, namely that the claim was not "fairly based on the matter disclosed in the specification" (section 32(l)(i)). The requirement of sufficiency was therefore regarded as serving a narrower purpose. But the disappearance of "lack of fair basis" as an express ground for revocation does not in my view mean that general principle which it expressed has been abandoned. The jurisprudence of the EPO shows that it is still in full vigour and embodied in articles 83 and 84 of the EPC, of which the equivalents in the 1977 Act are section 14(3) and (5) and section 72(l)(c).

81. Section 72(l)(c) can only give effect to this principle if the relevant date for compliance is the date of application. It would be illogical if a patent which ought to have been rejected under section 14(3) is rendered immune from revocation under section 72(1*)(c)* by advances in the art between the date of application and the publication of the specification. The provisions for amendment, so far from detracting from this view, seem to me to support it. Section 76(2) says that the amended application shall not disclose matter which extends beyond that previously disclosed. In other words, the application may not add new matter to make an insufficient application sufficient. It seems to me in accordance with this scheme that an insufficient application should also not become sufficient because of general developments in the state of the art after the filing date. I therefore agree on this point with the Court of Appeal.

82. I would dismiss the appeal.

Biogen Inc. (Appellants) v. Medeva plc (Respondents)

JUDGMENT

Die Jovis 31° Octobris 1996

Upon Report from the Appellate Committee to whom was referred the Cause Biogen Inc. against Medeva plc, That the Committee had heard Counsel as well on the 29th and 30th days of April as on the 1st, 2nd, 7th, 9th, 13th, 14th, 15th, 16th, 20th, 21st, 22nd and 23rd days of May last upon the Petition and Appeal of Biogen Inc., of 14 Cambridge Center, Cambridge, Massachusetts, United States of America, praying that the matter of the Order set forth in the Schedule thereto, namely an Order of Her Majesty's Court of Appeal of the 3rd day of November 1994, might be reviewed before Her Majesty the Queen in Her Court of Parliament and that the said Order

might be reversed, varied or altered or that the Petitioners might have such other relief in the premises as to Her Majesty the Queen in Her Court of Parliament might seem meet; as upon the case of Medeva plc lodged in answer to the said Appeal; and due consideration had this day of what was offered on either side in this Cause:

It is *Ordered* and *Adjudged,* by the Lords Spiritual and Temporal in the Court of Parliament of Her Majesty the Queen assembled, That the said Order of Her Majesty's Court of Appeal of the 3rd day of November 1994 complained of in the said Appeal be, and the same is hereby, **Affirmed** and that the said Petition and Appeal be, and the same is hereby, dismissed this House: And it is further *Ordered,* That the Appellants do pay or cause to be paid to the said Respondents the Costs incurred by them in respect of the said Appeal to this House, the amount thereof to be certified by the Clerk of the Parliaments if not agreed between the parties: And it is also further *Ordered,* That the fees and expenses payable to the Specialist Advisers appointed under Standing Order XIV be paid by both parties in equal shares.

Cler: Parliamentor: