HOUSE OF LORDS

OPINIONS OF THE LORDS OF APPEAL FOR JUDGMENT IN THE CAUSE

Conor Medsystems Incorporated (Respondents) *v* Angiotech Pharmaceuticals Incorporated and others (Appellants)

[2008] UKHL 49

LORD HOFFMANN

My Lords,

1. Angiotech Pharmaceuticals Inc, a Canadian company, and the University of British Columbia are joint proprietors of European patent 0 706 376 which claims, among other things, a stent coated with taxol for "treating or preventing recurrent stenosis". For convenience I shall call the patentees Angiotech. Conor Medsystems Inc (Conor), an American competitor, applied in both the United Kingdom and the Netherlands for revocation of the patent on the ground that the claimed invention was obvious. In the United Kingdom, before Pumfrey J and the Court of Appeal (Mummery, Tuckey and Jacob LJJ), it succeeded. In the Netherlands, before the District Court of The Hague (Robert van Peursem, Edgar Brinkman and Walter van Straalen) it failed. Angiotech appeals to your Lordships' House

cells in cancer tumours and might be treated by anti-proliferative drugs. Others favoured antithrombotic agents such as heparin, antiplatelet agents like aspirin, anti-inflammatories, calcium antagonists and lipid-lowering drugs. The article described two theories about how the process of restenosis took place. Both involved several stages at which different forms of pharmacological intervention might be appropriate.

7. The summary at the start of the second part of the article, which dealt with future possibilities, said:

> "[D]espite 15 years of clinical experience and research in the field of restenosis prevention, this has not yet resulted in the revelation of unequivocal beneficial effects of any particular drug. Other newer approaches likely to receive more attention in the future include anti-bodies to growth factors, gene transfer therapy and antisense oligonucleotides. Whether there is a feasible monotherapy, whether we have to focus on a drug combination, or whether we are only searching for the 'Holy Grail' remain to be answered."

8. Meanwhile in Vancouver, a young medical student named William Hunter was studying angiogenesis, the process by which capillary blood vessels grow, under a Dr Arsenault, who had made it his particular area of research. It occurred to Dr Hunter that one approach

from the Pacific yew tree, which was much in the news as a possible cancer treatment. Dissolved in cremophor for pharmacological use, it was marketed under the trade name of taxol. On the CAM assay, it appeared to have remarkable anti-angiogenic properties. Dr Hunter said it was effective to inhibit angiogenesis even in minute concentrations.

PCT Patent Application WO 91/12779 (Wolff) PCT Patent Application WO 93/11120 (Kopia) and an abstract of a paper by Katsuda and others delivered at a symposium in Rome in 1988 (Katsuda). I shall return to the prior art at the end of this opinion.

14. At the end of July and in early August 2005 Angiotech served reports from Professor Cumberland of Sheffield, an expert on cardio-vascular intervention, and Professor Calvert of Newcastle-on-Tyne, an oncologist. Conor's experts were Professor Rogers, a cardio-vascular specialist at Harvard, and Professor Lemoine, an oncologist at Barts. A reading of these reports suggests that the only issue over which the experts proposed to lock horns at the trial was whether it would have been obvious at the priority date to coat a stent with taxol to prevent or treat restenosis. Professor Rogers said that he would have consulted an oncologist about a suitable anti-proliferative drug. Professor Lemoine said that taxol was at the time a highly publicised new drug for cancer treatment. He would have recommended it and Professor Rogers said he would have found it attractive. On the other side, Professor Cumberland said that he would have seen no reason to select taxol out of the huge variety of possible solutions then under consideration and Professor Calvert said that, on account of its toxic properties, he would actually have advised against it.

15. That seemed a fairly straightforward issue and Angiotech no doubt prepared for trial clutching the Holy Grail paper as the best possible evidence that there was at the time no obvious solution to

16. On the basis that the patent taught no more than that taxol was worth trying, he submitted that it added nothing to existing knowledge. It was common ground that taxol was, like many other anti-proliferative drugs, worth a try. And that was obvious. It was not necessary for Conor to show that it was obvious actually to use taxol to treat restenosis because the patent did not teach that it would work.

17. I shall say at once that in my opinion this argument was an illegitimate amalgam of the requirements of inventiveness (article 56 of the EPC) and either sufficiency (article 83) or support (article 84) or both. It is the claimed invention which has to involve an inventive step. The invention means prima facie that specified in the claim: see section 125(1) of the 1977 Act. In the present case, the invention specified in claim 12 was a stent coated with taxol. There was no dispute that this was a new product. The question should therefore simply have been whether it involved an inventive step. As in the case of many product claims, there was nothing inventive in discovering how to make the product. The alleged inventiveness lay in the claim that the product would have a particular property, namely, to prevent or treat restenosis. (Compare *Pharmacia Corp v Merck & Co Inc* [2002] RPC 775). So the question of obviousness was whether it was obvious to use a taxol-coated stent for this purpose. And this, as I have said, was the question to which the experts addressed themselves.

18. Mr Thorley, however, sought to

> humans and the actual prevention of restenosis be included in the patent to further substantiate [the claim]."

20. There seems to have been no dispute about what the experts thought the teaching of the patent to be. In cross-examination, Mr Thorley put to Professor Cumberland:

> "Q. The teaching on page 12, lines 33-38 [of the patent in suit] , is that an anti-angiogenic composition can be used to treat restenosis. Correct, professor?
>
> A. Either prevent or treat.
>
> Q. Prevent or treat."

21. That speaks in general terms of anti-angiogenic compounds and it

> illustrated such an event. By being arrested in mitosis, endothelial cells could not undergo their normal metabolic functions involved in angiogenesis. In comparison, the avascular zone formed by suramin and cortisone acetate do not produce mitotically arrested cells in the CAM; they only prevented further blood vessel growth into the treated area. Therefore, even though agents are anti-angiogenic, there are many points in which the angiogenesis process may be targeted.
>
> We also observed the effects of taxol over the 48 hour duration and noticed that inhibition of angiogenesis occurs as early as 9 hours after application. … Also, we observed the revascularization process into the avascular zone previously observed. It has been found that the avascular zone formed by heparin and angiostatic steroids became revascularized 60 hours after application. In our study, taxol-treated avascular zones did not revascularize for at least 7 days after application implying a more potent long-term effect."

22. It is true that the specification said very little about the details of how or why taxol would be efficacious in preventing restenosis. It clearly saw the solution for restenosis in terms of preventing angiogenesis, but offered no proof that this was right. In cross-examination, Mr Thorley put to Professor Cumberland (Day 3, p.517):

> "Q. The disclosure that a compound is anti-angiogenic would be of no assistance to you in concluding whether that compound would actually work to inhibit the proliferation of smooth muscle cells?
>
> A. That is correct, at that time, yes."

23. That again meant that the patentee appeared to be at risk of a finding of insufficiency. On the other hand, if (as turned out to be the case) the invention did work, it would not matter why. The reason may have had nothing to do with anti-angiogenesis. The specification would be sufficient if, for whatever reason, taxol coated stents possessed the claimed property of preventing or treating restenosis.

24. Likewise, Mr Thorley elicited a string of admissions from Professor Cumberland about whether the specification provided enough information to enable the skilled person to make a suitable stent:

> "Q. There is no data in this patent which demonstrates that any of those compounds actually worked to treat restenosis?
>
> A. That is correct.
>
> Q. The patent does not address the question of whether any of the compounds will inhibit the proliferation of smooth muscle cells?
>
> A. That is correct.
>
> Q. It does not address the question of whether local administration of any of the compounds will cause unmanageable side-effects?
>
> A. I think that is correct, yes.
>
> Q. The patent does not address the question of the dose of drug that will be needed to prevent or cure restenosis?
>
> A. That is true.
>
> Q. lt does not address the question of the period of time for which the drug should rest at the location in question?
>
> A. True. That is correct."

25. At this point, Mr Waugh objected that these questions appeared to go to the question of sufficiency rather than obviousness. The judge disagreed, saying afterwards in his judgment (at paragraph 27) that this evidence showed that the disclosure was merely a speculative idea. In my opinion, however, Mr Waugh's point was well taken. The questions had nothing to do with whether claim 12 involved an inventive step.

26. In his judgment, Pumfrey J accepted Mr Thorley's argument. He said:

> "61. In summary, therefore, the Claimant's case is that it is sufficient for the purposes of invalidating the claims of the patent in suit that the interventional cardiologist, in consultation with someone of skill and experience in the field of anti-mitotic drugs of one sort or another, would see paclitaxel (taxol) as worth experimentation. The

Patentees' case is that the properties of taxol are such that the skilled person would not think that it was suitable for local administration in a drug-eluting stent. The Patentees' contentions centre on the toxic character of taxol. It is therefore necessary at this point to deal with a particular question which has vexed this case. Is it sufficient for Conor to show that taxol is an obvious candidate for testing on a drug-eluting stent in addition to the material specifically identified in Wolff, or is it necessary to show that taxol is an obvious, or the obvious, material to use in a drug-eluting stent for administration to human beings? Put another way, is the patent vulnerable only if it can be shown that the skilled person would have an expectation of success sufficient to induce him to incorporate taxol in a drug-eluting stent, or is it sufficient that without any expectation of success he would test or screen taxol?

62. In my judgment, this question is to be answered by assessing the contribution to the art disclosed by the specification. For the reasons that I have given above, I am satisfied that the disclosure of the specification is that taxol may be incorporated in a stent. It does not suggest that such a stent would be safe or that such a stent would work to prevent restenosis. I think it is fair to say that the sum of the disclosure of the specification is that taxol should be incorporated in a drug-eluting coating on a stent with a view to seeing whether it works to prevent restenosis and whether it is safe. If it is obvious to the skilled person that taxol should be incorporated in a drug-eluting coating on a stent with a view to seeing whether it prevents restenosis and is safe, then the claim is invalid, the specification having made no contribution to the art. It is obviously preferable to identify the correct question before assessing the evidence. In this case, the profound difference between the parties as to the nature of the inventive step has led them to identify as relevant very different factors.

64. The claim is to a physical device, that is, to a stent upon which is a drug-eluting coating loaded with taxol and optionally with other active ingredients as well. If, as I consider is the case here, the specification provides directions to make such a stent, but provides no data or other material suggesting that such a stent is in fact suitable for the treatment of restenosis, then success in

preventing restenosis is not, in my view, a relevant consideration when assessing the obviousness of constructing such a stent. I accept immediately that there

38. The issue in the Court of Appeal appears to have been whether the teaching of the patent was that a taxol-coated stent would prevent or treat restenosis. Jacob LJ disagreed with the view of the Dutch court, which I have already quoted, that that was precisely what the patent said. He said that the Dutch court had formed its view "with the hindsight knowledge that taxol stents work". I do not think that this is a fair criticism. The Dutch court was not addressing itself to whether taxol worked, or whether the specification proved that it would work, but to whether the specification taught that it should be used. And it did so by reference to the disclosure of the success of taxol in the CAM assay and the specific references to taxol in the claims. Jacob LJ considered that there was nothing in these points. After reading part of the passage about the CAM assay which I have quoted above, he said:

> "But this is miles away from indicating that taxol is a particularly suitable anti-angiogenic for a drug eluting vascular stent or that the CAM assay is a test for a drug which will actually work to prevent restenosis in a drug eluting vascular stent."

39. If, by using the word "indicating", Jacob LJ meant "proving", then of course I agree. The specification did not prove that taxol would work. If, however, he meant that it did not claim that taxol would work, then I would regard it as a very narrow approach to the meaning of the patent, more suitable to old-fashioned statutory construction than to what the skilled practitioner in cardio-vascular intervention would have understood. It was, as appears from Mr Thorley's question to Professor Cumberland, common ground that that the teaching of the patent was to use an anti-angiogenic factor on a stent to prevent or treat restenosis. The disclosure of the results of the CAM assay taught that taxol was the best anti-angiogenic. I do not understand what more the patentee could have said.

40. In the event, therefore, neither the judge nor the Court of Appeal answered what I consider to have been the correct question, namely, whether it was obvious to use a taxol-coated stent to prevent restenosis. One can however, deduce the answer which Pumfrey J would have given to this question from the way in which he formulated the issue which he had to decide. It was, at the end of the passage I have quoted:

> "is the patent vulnerable only if it can be shown that the skilled person would have an expectation of success sufficient to induce him to incorporate taxol in a drug-eluting stent, or is it sufficient that without any expectation of success he would test or screen taxol?"

41. The judge answered this question in the second sense, from which I think it can be inferred that he would have rejected the attack on the patent if he had answered it in the first and in my opinion correct sense. That, in my view would have been inevitable. Of the three cited items of prior art, both Wolff and Kopia are concerned with methods of delivery. In the case of Wolff, it is by a drug eluting stent and in the case of Kopia it is by chemical means. But neither of them identifies taxol as particularly suitable. Wolff does not mention it except by implication in a generic reference to anti-proliferatives and although Kopia does mention it, it is one of an undifferentiated number of drugs which could be tried. The disclosures leave one in no better position than a reader of the Holy Grail article, namely, with the knowledge that the solution may lie somewhere in the large number of drugs which could be tried. Katsuda, the last item of prior art, discloses in vitro work which showed that taxol prevented mitogenic proliferation (ie growth by cell division) of smooth muscle cells. That also seems to me insufficient to make it obvious that taxol would prevent restenosis.

42. In the Court of Appeal, Jacob LJ dealt comprehensively with the question of when an invention could be considered obvious on the ground that it was obvious to try. He correctly summarised the authorities, starting with the judgment of Diplock LJ in *Johns-Manville Corporation's Patent* [1967] RPC 479, by saying that the notion of something being obvious to try was useful only in a case in which there was a fair expectation of success. How much of an expectation would be needed depended upon the particular facts of the case. As Kitchin J said in *Generics (UK) Lt*

> processes being common to many industries, these documents, although addressed primarily to the mining and paper industries respectively, were likely to be read by those concerned with the asbestos cement industry, and that such readers would have realised that here was a newly-introduced flocculating agent which it was well worth trying out in their own filtration process. I can see no grounds which would justify this court in reversing this concurrent finding by two expert tribunals."

Diplock LJ was not here expounding a technical doctrine. On the contrary, he was at pains to stress the need to avoid generalisation. A little earlier in his judgment he had said (at pp 494-495):

> "I have endeavoured to refrain from coining a definition of 'obviousness' which counsel may be tempted to cite in subsequent cases relating to different types of claims. Patent law can too easily be bedevilled by linguistics, and the citation of a plethora of ca

> of patentees and applicants on the one hand and patent offices and national courts on the other. A company which has spent millions of dollars on research and has produced a valuable new drug will be understandably irritated when, say, a court declares the patent invalid for obviousness, thereby opening up the market to competitors who are free to copy. That irritation is likely to be particularly acute when the raison d'être of the patent system is said to be the economic encouragement of research and development.
>
> The problems can be approached by considering first the concept of 'obvious to try'. The classic statement of this principle is set out in the judgment of the Court of Appeal in *Johns-Manville Corporation's Patent*. It was said that a development should be treated as obvious if 'the person versed in the art would assess the likelihood of success as sufficient to warrant actual trial'. Statements to similar effect have been made by the EPO.
>
> On its face, this produces an unworkable or irrational test. If the reward for finding a solution to a problem and securing a monopoly for that solution is very high, then it may well be worthwhile for large players to examine all potential avenues to see if one gives the right result, even though the prospects of any one of them succeeding are much less than 50/50. What makes something worth trying is the outcome of a simple risk to reward calculation. Yet, if the reward is very large, the avenues worth trying will be expanded accordingly. So, the more commercially attractive the solution and the more pressing the public clamour for it, the harder it will be to avoid an obviousness attack. In those circumstances a solution which is quite low down a list of alternatives, all of which are more or less worth trying, will fail for obviousness; a consequence which is consistent with the decision in *Brugger v Medic-Aid*."

Sir Hugh goes on to suggest that as technology advances rapidly, this is a serious and growing problem.

49. In the Court of Appeal in this case Jacob LJ (paras 39-45) made some comments to the same general effect, with a useful anthology of citations from different jurisdictions.

Grail" paper published in 1993. The specification, fairly construed, did put forward a taxol-eluting stent as the answer to this problem. But that teaching had to be disentangled from so much extraneous matter that it nearly got lost.

BARONESS HALE OF RICHMOND

My Lords,

54. For the reasons given by my noble and learned friend, Lord Hoffmann, with which I agree, I too would allow this appeal.

LORD NEUBERGER OF ABBOTSBURY

My Lords,

55. I have had the benefit of reading in draft the opinions of my noble and learned friends Lord Hoffmann and Lord Walker of Gestingthorpe. I agree with them that this appeal should be allowed. Although the decision represents a significant development in United Kingdom patent law, and we are differing from the views of highly experienced Judges in that field, I do not think there is anything that I can usefully add to the reasons given by Lord Hoffmann, or to the additional remarks of Lord Walker, with both of whom I entirely agree.