

Neutral Citation Number: [2007] EWCA Civ 5

Case No: A3/2006/0657

IN THE SUPREME COURT OF JUDICATURE
COURT OF APPEAL (CIVIL DIVISION)
ON APPEAL FROM CHANCERY DIVISION PATENTS COURT
MR JUSTICE PUMFREY
HC05C00376 – [2006] EWHC 260 (Pat)

Royal Courts of Justice
Strand, London, WC2A 2LL

16th January 2007

Before:

LORD JUSTICE MUMMERY
LORD JUSTICE TUCKEY
and
LORD JUSTICE JACOB

Between:

ANGIOTECH PHARMACEUTICALS & ANR.	<u>Appellant</u>
- and -	
CONOR MEDSYSTEMS Inc	<u>Respondent</u>

(Transcript of the Handed Down Judgment of
WordWave International Ltd
A Merrill Communications Company
190 Fleet Street, London EC4A 2AG
Tel No: 020 7421 4040 Fax No: 020 7831 8838
Official Shorthand Writers to the Court)

Andrew WAUGH Q.C. and Colin BIRSS (instructed by **Messrs Taylor Wessing**) for the
Appellants
Simon THORLEY Q.C. and Thomas HINCHLIFFE (instructed by **Messrs Simmons &**
Simmons) for the **Respondents**

Hearing dates: 12th, 13th, 14th December 2006

Judgment

Lord Justice Jacob:

1. The patentees, Angiotech and the University of British Columbia, appeal the decision of Pumfrey J [2006] EWHC 260 (Pat) that their EP (UK) 706376 is invalid for obviousness. They do so with the Judge's permission. Mr Andrew Waugh QC and Mr Colin Birss argued the case for Angiotech, Mr Simon Thorley QC and Mr Thomas Hinchliffe that for the Respondents, Conor.
2. Appeals on obviousness face the particular hurdle that it must be shown the Judge was wrong which in turn involves showing that he made some error of principle – see *Biogen* [1997] RPC 1 at 45 which I do not set out here.
3. Pumfrey J provided a useful introduction by way of background to the technology, all of which is uncontroversial and there is no point in my doing other than borrowing wholesale and with gratitude:

“[4] Coronary heart disease is caused by a narrowing or blockage of the coronary arteries, whose task is to supply the heart muscle with blood. Arterial walls have three layers: a thin inner layer called the intima; a middle layer called the media, which consists of muscle; and an outer layer called the adventitia, which is a loose layer of connective tissue. The normal cause of arterial narrowing is atherosclerosis, in which a gradual build-up of fatty material in the inner layer of the artery wall takes place. This build-up of fatty material is followed by a deposit of fibrous tissue which produces a plaque protruding into the channel of the artery. The narrowing caused by the plaque is called a stenosis. The channel of the artery is referred to as the lumen, and as the lumen becomes progressively narrowed, the heart muscle becomes deprived of blood when demands are made of it, for example during exercise. The patient may then complain of angina, which is typically a crushing or constricting sensation in the chest and which may spread elsewhere, for example in the left arm or neck. If the protective fibrous cap on the surface over the fat-laden core of the plaque (the so-called atheroma) breaks, the platelets in the bloodstream adhere to the roughened exposed surface and a blood-clot forms. Any angina may worsen and, if the lumen of the artery is suddenly closed off, blood-flow ceases and the heart muscle dies, resulting in a heart attack.

[5] By the mid 1980s, there were three ways of treating coronary heart disease: drugs, coronary bypass surgery and angioplasty. Drugs may be used to relieve the symptoms of angina by relaxing the muscle of the artery wall, which improves the supply of blood to the heart muscle. They may also be used to make the heart beat less forcefully, so reducing its workload. Clot-dissolving drugs may be used, as may anti-platelet drugs, which reduce the tendency of the platelets to adhere to the plaques. (Platelets are specialised cells responsible for clotting.) If drugs alone are insufficient, and

there is narrowing and blockage in several arteries, the patient may undergo coronary artery bypass surgery, in which vessels from elsewhere in the patient's body are used to bypass the problem by connecting them round the blockage. This surgery can relieve angina and may be successful for many years if the grafts remain open. Angioplasty is a technique originally developed in the early 1960s, but whose application to the coronary arteries became possible after the development of a balloon which, when inflated, was strong enough to dilate an arterial stenosis in a coronary artery. One Andreas Grüntzig developed a catheter with a relatively non-elastic sausage-shaped balloon near its tip. The catheter had two channels: one for introducing a guide-wire along which the balloon catheter could be passed and the other carrying fluid at a high pressure (between 6 and 12 bar) to inflate the balloon. The catheter is inserted in one of the main arteries, normally in the groin or in the arm, and manoeuvred to the site of the stenosis by the operator, who observes its progress using radiological techniques.

[6] The first percutaneous angioplasty was performed in 1977. The idea is that, once the wire is in place and the balloon passed into position along it, the balloon is then inflated so as to expand the lumen at the point of the stenosis. The procedure was and is successful, and in many cases relieves the patient of the burden of a bypass operation. It has low morbidity, rapid recovery time, and is repeatable. It is minimally invasive and does not require a general anaesthetic. It appears to have rapidly gained ground in the 1980s and by the middle of that decade had become widely accepted as an alternative to bypass surgery.

[7] By the mid 1980s it was becoming clear that there were problems associated with balloon angioplasty. Two in particular are important. The first, acute closure, took place in between 5% and 10% of patients. It occurred as the catheter was withdrawn. Without quick reaction by the operator, backed up if need be by emergency bypass surgery, acute closure would be fatal to the patient. The other problem is the gradual closure of the lumen, known as restenosis. Restenosis occurs in 33% to 50% (or possibly more) of patients. It normally takes place within six months following the angioplasty procedure, and is likely to re-occur at the same sort of rate among patients who had second and subsequent angioplasties. There is no doubt that restenosis was and remains a serious problem with the balloon angioplasty procedure.

[8] The attempt to deal with this problem has passed through a number of stages. The first was the employment of

coronary stents. Stents are devices inserted into the diseased artery at the point at which the balloon expanded to open the lumen. They act as scaffolding to hold the artery open. The desirability of stenting had been obvious from the early days of balloon angioplasty, but real success only came with the use of stents that were themselves held on the balloon and expanded with it so as to be automatically placed in the right position during the procedure. A number of expandable core stents were developed from the mid 1980s onwards and were used from the late 1980s to see if they might reduce restenosis – they are obviously useful in preventing acute closure. Nonetheless, patients who had received a stent still suffered restenosis, and the reduction in restenosis rates was investigated. Two studies suggested that there was still a very significant rate of restenosis in patients receiving a balloon expandable stent in angioplasty.”

4. The priority date of the patent is 19th July 1993. Identical amendments to it were allowed by the Opposition Division of the EPO and Pumfrey J. Although Angiotech formally maintained that claims 1, 6 and 12 were independently valid, the real debate has been about claim 12 and particularly that aspect of it concerned with vascular stents. There is no dispute that if claim 12 fails, the wider claims must fail too.

5. Pumfrey J set out the material claims at [25]:

“1. A stent for expanding the lumen of a body passageway, comprising a generally tubular structure coated with a composition comprising an anti-angiogenic factor and a polymeric carrier, the factor being anti-angiogenic by the CAM assay, and wherein said anti-angiogenic factor is taxol, or an analogue or derivative thereof.

.....

6. A stent according to any one of claims 1 to 5 wherein said stent is a vascular stent.

.....

[11. A stent according to any one of claims 1 to 5 for treating narrowing of a body passageway.]

12. A stent according to claim 11 for treating or preventing recurrent stenosis.”

6. Claim 12 can therefore be written out without the dependencies in this way:

“A stent

for expanding the lumen of a body passageway,

comprising a generally tubular structure coated with

a composition comprising an anti-angiogenic factor and a polymeric carrier, the factor being anti-angiogenic by the CAM assay,

and wherein said anti-angiogenic factor is taxol, or an analogue or derivative thereof,

for treating narrowing of a body passageway,

for treating or preventing recurrent stenosis.”

7. This is clumsy wording, arising in part from the process of amendment. What really matters, and what the dispute is about, is whether a vascular stent in accordance with this claim is obvious.

The Patent

8. As originally drawn the patent cast its disclosure and claimed monopoly much, much wider than vascular stents coated with taxol in a carrier. Indeed its opening words are mainly about cancer treatment:

“Technical field

The present invention relates generally to compositions and methods for treating cancer and other angiogenic-dependent diseases, and more specifically to compositions comprising anti-angiogenic factors and polymeric carriers, stents which have been coated with such compositions, as well as methods for utilizing these stents and compositions”

9. The Judge rightly observed that “very little of [the patent] is about restenosis and stents”. Having set out those opening words he went on to summarise the relevant parts of the disclosure as follows:

“[13] “‘Angiogenesis’ is the term employed to refer to the growth of blood vessels. The basic idea, as expressed in this paragraph, is to inhibit the growth of tissue by preventing the formation of blood vessels. The background of the invention is described, in a lengthy passage from page 2₁₁ to 3₃₉, in terms of cancerous tumours. A passage of some importance is at page 3₁₃₋₂₁, as follows:

‘A related problem to tumor formation is the development of cancerous blockages which inhibit the flow of material through body passageways, such as the bile ducts, trachea, esophagus, vasculatures and urethra. One device, the stent, has been developed in order to open passageways which have been blocked by tumors or other substances. Representative examples of common stents include the Wallstent, Strecker stent, Gianturco stent and the Palmaz

stent. The major problem with stents, however, is that they do not prevent the ingrowth of tumor or inflammatory material through the interstices of the stent. If this material reaches the inside of a stent and compromises the stent lumen, it may result in blockage of the body passageway into which it has been inserted. In addition, presence of a stent in the body may induce reactive or inflammatory tissue (e.g. blood vessels, fibroblasts, white blood cells) to enter the stent lumen, resulting in partial or complete closure of the stent.’

The patent then sets out at page 3₃₀ what is described as a summary of the invention. This is no longer an accurate description of the passage which follows, since very extensive amendments to the claims have been permitted by the EPO. Since the various formalities relating to amendment had not been completed before the trial of the action before me, I made an order amending the patent in the same way as had been authorised by the EPO. In the result, it will be observed that at many places in the body of the specification the word “invention” has been replaced by the word “disclosure”, since much of the descriptive matter has become irrelevant to the granted claims, other than as background or as statements of technical fact relating to related matters.

[14] As amended, the passage at page 3₃₂₋₃₉ accurately sets out the concept underlying the invention claimed by claims 1 to 12 as amended:

‘Briefly stated, the present disclosure relates to anti-angiogenic compositions, as well as methods and devices which utilize such compositions for the treatment of cancer and other angiogenesis-dependent diseases. Compositions are disclosed (hereinafter referred to as “anti-angiogenic compositions”) comprising (a) an anti-angiogenic factor and (b) a polymeric carrier. Molecules which are utilized within the scope of the present invention as anti-angiogenic factors are taxol, taxol analogues and taxol derivatives. Similarly, a wide variety of polymeric carriers may be utilized . . .’

[15] Stenting is described at page 3₄₈ as follows:

‘According to the present invention, there is provided a stent in accordance with claim 1. Within other aspects of the present invention, such stents are provided for use in a method of expanding the lumen of a body passageway, comprising inserting a stent into the passageway, the stent having a generally tubular structure, the surface of the structure being coated with an anti-angiogenic composition as described above, such that the passageway is expanded. Within various embodiments of the invention, such methods

include eliminating biliary obstructions, comprising inserting a biliary stent into a biliary passageway; eliminating urethral obstructions, comprising inserting a urethral stent into a urethra; eliminating esophageal obstructions, comprising inserting an esophageal stent into an esophagus and eliminating tracheal/bronchial obstructions, comprising inserting a tracheal/bronchial stent into the trachea or bronchi. In each of these embodiments, the stent has a generally tubular structure, the surface of which is coated with an anti-angiogenic composition as described above.’

Then, after dealing with corneal neovascularisation after cancer surgery, a method of manufacturing a medicament for treating arthritis is disclosed. A similar passage to that which I have already quoted above is set out at page 4₁₂₋₁₉, but specifying taxol, and, with that introduction, the specification turns to a brief description of the drawings, which precedes in the usual way the detailed description of the invention.

[16] The detailed description begins with a description of an assay for suitable anti-angiogenic compounds. The claim now being limited to taxol, this is of importance only to understanding the manner in which the claims are constructed, since they refer to the “CAM” assay. This assay, which is described in detail later on in the specification, is an assay to determine whether a particular compound inhibits vascular growth *in vivo*. The assay is simple enough: it utilizes the vascularisation of a chick embryo as it grows within the shell. The specification turns to compositions comprising an anti-angiogenic compound and a polymeric carrier at page 6₃, a passage in which taxol is not distinguished from other materials of this description. Taxol is again discussed at page 6₂₄, where it is described in more detail:

‘Taxol is a highly derivatized diterpenoid . . . which has been obtained from the harvested and dried bark of *Taxus brevifolia* (Pacific Yew) and *Taxomyces Andreanae* an[d] *Endophytic Fungus* of the Pacific Yew . . . Generally, taxol acts to stabilize microtubular structures by binding tubulin to form abnormal mitotic spindles. “Taxol” (which should be understood herein to include analogues and derivatives of taxol such as, for example, baccatin and taxotere) may be readily prepared utilizing techniques known to those skilled in the art . . . or obtained from a variety of commercial sources, including for example, Sigma Chemical Co., St Louis, Missouri . . .”

[17] It is not necessary to deal with the discussions of Suramin and Tissue Inhibitor of Metalloproteinases-1 or Plasminogen Activator Inhibitor, which follow the passage relating to taxol. At page 6₅₂ the specification states that “a

wide variety of other anti-angiogenic factors may also be utilized within the context of the present disclosure". Two of these materials in particular are to be noted – Methotrexate (page 7₂) and Heparin (page 7₄). The evidence was that Methotrexate was not positive in the CAM assay, a fact which had been established by tests carried out by the Patentees. It had also been shown (along with Heparin) not to prevent restenosis in a study in pigs using drug-eluting stents carried out by Cox some two years previously.

[18] The nature of the polymeric carrier is described at page 7₃₇, from which it will be seen immediately that a huge range of different polymers is within the Patentees' contemplation. At page 7₅₅ there is some indication of the manner in which a polymeric carrier is to be selected, but the directions given are so general as to throw the skilled reader back onto the relevant common general knowledge:

‘Preferably, anti-angiogenic compositions for use in the present invention (which comprise one or more anti-angiogenic factors, and the polymeric carrier) are fashioned in a manner appropriate to the intended use. Within preferred aspects of the present invention, the anti-angiogenic composition should be biocompatible, and release one or more anti-angiogenic factors over a period of several weeks to months. In addition, anti-angiogenic compositions of the present invention should preferably be stable for several months and capable of being produced and maintained under sterile conditions.’

[19] A number of other presentations are also discussed. They are polymer spheres or microspheres; sprayable nanoparticles; paste or gel; or films. Having regard to the field of application of the present invention, it comes as something of a surprise to find that the first application of the invention is in arterial embolization: that is, the obstruction of a blood vessel to prevent the supply of blood to a tumour. The field of application of this technique is stated to be wide and it is discussed in detail in the passage from page 8₃₃ to page 10₂₅, where the disclosure then turns to the use of anti-angiogenic compositions as coatings for stents.

[20] The specification describes stents in a general way, and sets out a number of relevant US patents. It describes coating the stents with both anti-angiogenic compositions (i.e. polymer/drug compositions) and anti-angiogenic factors themselves. Again, the directions are very general:

‘Within preferred embodiments of the invention, the composition should firmly adhere to the stent during storage and at the time of insertion, and should not be dislodged

from the stent when the diameter is expanded from its collapsed size to its full expansion size. The anti-angiogenic composition should also preferably not degrade during storage, prior to insertion, or when warmed to body temperature after expansion inside the body. In addition, it should preferably coat the stent smoothly and evenly, with a uniform distribution of angiogenesis inhibitor, while not changing the stent contour. Within preferred embodiments of the invention, the anti-angiogenic composition should provide a uniform, predictable, prolonged release of the anti-angiogenic factor into the tissue surrounding the stent once it has been deployed. For vascular stents, in addition to the above properties, the composition should not render the stents thrombogenic (causing blood clots to form), or cause significant turbulence in blood flow (more than the stent itself would be expected to cause if it was uncoated).’

[21] The use of expandable stents in the lumens of a variety of body passageways for the purpose of eliminating obstruction is described. The first example is the biliary system, in which the troublesome obstructions described are all tumour-induced. The same goes for the examples given of the use of the stent in the oesophagus, the trachea, the bronchi and the urethra. Finally, at page 12₃₂ is the comparatively brief passage which describes the invention so far as it has found application in therapy:

‘Within another embodiment of the disclosure, methods are provided for eliminating vascular obstructions, comprising inserting a vascular stent into a blood vessel, the stent having a generally tubular structure, the surface of the structure being coated with an anti-angiogenic composition as described above, such that the vascular obstruction is eliminated. Briefly, stents may be placed in a wide array of blood vessels, both arteries and veins, to prevent recurrent stenosis at the site of failed angioplasties, to treat narrowings that would likely fail if treated with angioplasty, and to treat post surgical narrowings (e.g. dialysis graft stenosis). Representative examples of suitable sites include the iliac, renal and coronary arteries, the superior vena cava, and in dialysis grafts.’

[22] There is some general teaching of the mode of operation of the anti-angiogenic compositions at page 14₂₂, a short passage which observes that the compositions block the stimulatory effects of angiogenesis promoters, reducing endothelial cell division, decreasing endothelial cell migration and impairing the activity of the proteolytic enzymes secreted by the endothelium. This passage seems to me to relate to the corneal endothelium alone.

[23] After a brief diversion into hypertrophic scars and keloids, the specification returns to the eye at page 15₁₀ with a discussion of neovascular glaucoma, followed by diabetic retinopathy and retrolental fibroblasia. The specification turns then to rheumatoid arthritis and the coating of vascular grafts. There is no further discussion of the use of stents.

[24] A very extensive set of examples is provided between pages 17 and 37. Example 2 describes the CAM assay and the employment of that assay in assessing taxol. The conclusion in relation to taxol is that it clearly inhibits angiogenesis by arresting endothelial cells in mitosis. Example 7 describes the use of biliary stents in rats to inhibit tumour in-growth, without stating what the anti-angiogenic factor employed was. Taxol is used as the exemplar for the manufacture of microspheres in example 8 and for the manufacture of a stent coating in example 9. The use of the CAM assay in assessing the release of taxol from microspheres is discussed in example 12 and its use in polymeric films in example 13. It is the anti-angiogenesis factor employed in example 15 (assessment of a taxol-loaded paste in the CAM assay) and in example 16 (use of a taxol-loaded paste to inhibit tumour growth and tumour angiogenesis in mice). In example 17 the effect of the taxol-loaded paste in another mouse tumour model is assessed. Example 18 describes the use of films loaded with 5% taxol for use in surgery. The idea is that during resection of a tumour the film may be used to protect adjacent organs from inadvertent contamination by cancer cells, and possibly left *in situ* to provide continued protection. Finally, example 19 is concerned with the treatment of rheumatoid arthritis using taxol-loaded microspheres. This is a summary, but I believe a sufficient summary, which shows that there is no example of the use of taxol-coated stents for the inhibition of restenosis at angioplasty sites.”

10. The Judge considered the elements going to make up claim 12, saying this:

“[26] It is common ground that taxol is in fact anti-angiogenic by the CAM assay. Those words therefore do not add anything to claim 1 if for any reason it is obvious to employ taxol on a stent suitable for expanding the lumen of a body passageway. Nor has it been suggested that success in the CAM assay is either necessary or sufficient for a material to be suitable for preventing restenosis. So far as claim 6 is concerned, it is, I think, assumed by both parties that it is possible to identify vascular stents as a particular class of stent, and it seems to me that claim 12 adds nothing to claim 6 as a matter of inventive concept, although the word “recurrent” is perhaps not what was intended: I read claim 12 as stating that

the stent must be suitable for treatment or prevention of stenosis.”

The inventive concept of claim 12

11. Mr Waugh submitted that the Judge was in error here – that “treating or preventing restenosis” was in some way more limiting than “suitable for treatment or prevention of stenosis.” I do not really understand the point he was trying to make. Stenosis is the narrowing of the passageway. When the passageway is widened by angioplasty a stent is put in with a view to stopping it narrowing again (“restenosing”). But despite the stent, restenosing may occur. The taxol is intended to stop that– to stop stenosis happening again after the stent is put in. That is what the word “recurrent” clearly means in context. And the judge is not saying anything different when he said that the stent “must be suitable for treatment or prevention of stenosis” – for ex hypothesi when the stent is inserted, there has already been a stenosis. This point goes nowhere.
12. Mr Waugh also submitted that the requirement of being anti-angiogenic by the CAM assay was an important part of the claim. I do not understand that. Actually it adds nothing at all to the scope of the claim. For taxol is anti-angiogenic by the CAM assay. To specify “an anti-angiogenic factor which is anti-angiogenic by the CAM assay” and that that factor is taxol, is just a long-winded way of saying “taxol”. The curious elaborate language is just an artefact of the amendment process.
13. Mr Waugh finally submitted that the Judge made an error in not paying attention to the closing words of the claim *for the purpose of ...* He suggested they meant “suitable for the purpose of” and somehow that made a difference to the concept. He is of course right that the words do add the requirement of suitability for purpose. But I cannot see why this supposed difference matters or where the Judge is supposed to have gone wrong. No doubt too much or too little taxol may have the effect of making a taxol eluting stent unsuitable for the purpose. But that is irrelevant to obviousness. I do observe, however, that it cannot really lie in the patentee’s mouth to say that its concept was the realisation that any particular concentration or content of taxol would make a stent “suitable for etc.” since he gives no information about any such content or concentration.
14. Mr Waugh made a separate point about the CAM assay to which I must return. At this point it sufficient to say that the Judge made no error of construction. The heart of the claim is to a stent coated with a polymer containing taxol such that it is suitable to prevent or treat stenosis after insertion. That is the inventive concept of the claim.

The Common General Knowledge

15. The obviousness or otherwise of the claim falls to be considered by first learning and understanding the common general knowledge (“cggk”) of the persons skilled in the art. The parties were agreed that so far as the patent is concerned with the problem of restenosis in vascular arteries, that “person” would be a team engaged in research aimed at treating or more particularly preventing restenosis after angioplasty. The team would particularly include an interventional cardiologist and someone familiar with drugs for treating cancer.

16. In addition to the matter recited by the Judge in his paragraphs [4]-[8], the Judge found the following to be cgk at [54]:
- “(a) Bare metal stents were available for use with balloon angioplasty in the treatment of atherosclerosis. There were problems with the deliverability of stents in coronary arteries.
 - (b) Restenosis was known to occur as a result both of balloon angioplasty and of stenting.
 - (c) Restenosis was known to be caused by (*inter alia*) the proliferation of smooth muscle cells.
 - (d) Research was known to be directed (*inter alia*) into local delivery of anti-proliferative drugs.
 - (f) One form of delivery being contemplated was in the form of a drug-eluting stent. Dosage levels of drugs to be used on drug-eluting stents were of orders of magnitude lower than those used for systemic administration.
 - (g) The concept of using a polymer coating on the stent as a vehicle for drug delivery was well known.
17. Mr Waugh sought to challenge findings (g) and, I think (f) also. It was an odd sort of attack because there was ample evidence to support the findings. What Mr Waugh submitted was that this knowledge should not be regarded as part of the skilled man’s mental toolkit because he would not take these ideas as sufficiently established to be a basis on which he could proceed: “you do not put something in your mental toolkit unless you have a good sense that it works.”
18. There is no substance in this attack. “Common general knowledge” is not formulaic – it is a term used in patent law to describe what the notional skilled person would know and take for granted. If the evidence shows that he knows people are looking at drug eluting stents as a way forward, then even if that has not been proved to work, it is nonetheless part of his mental equipment, not on the basis that he knows that it will work but on the basis that it may.
19. Next there is the common general knowledge of taxol itself. It was well-known to oncologists as an anti-replicate. It was known to be extremely insoluble in water and had been reported as having cardiac toxicity. The Judge sets out the common general knowledge of taxol in more detail at [66 -67] and it is not necessary to say more here.
20. Although it is already covered by item (b) of the cgk summarised by the judge he made more specific findings about the problem of restenosis. He said:
- “[53] In summary, therefore, the problem of restenosis was a problem that had been identified in the early years of balloon angioplasty. Stenting had begun in about 1985 and the first reported instance of restenosis appears, as I understand it, in a paper by Sigwart in about 1988.”

21. And he accepted as ckg a passage from a paper by Herrman and others (“the Holy Grail Paper”) the following:

“After the disruptive action of balloon dilatation, smooth muscle cells respond by proliferation. Cell characteristics shift from the contractile to the synthetic phenotype, which results in an intracellular matrix deposition. Since one of the key features of restenosis is the uncontrolled proliferation of vascular smooth muscle cells, anti-proliferative agents have been considered as an attractive concept.”

Wolff (PCT Appn. WO 91/12779)

22. There is no complaint about the Judge’s description of this citation, which I can therefore repeat verbatim:

[57] Wolff was published on 5th September 1991. This is about two years before the priority date of the patent in suit. Wolff was employed by Medtronic, a company engaged heavily in this class of research. It is entitled “Intraluminal Drug Eluting Prosthesis”. Wolff is concerned with intravascular stents, as its title suggests. The patent begins with a statement that the invention relates to methods of lessening restenosis of body lumens, and to prostheses for delivering drugs to treat said restenosis, and turns immediately to a description of the related art. This description is important for the context of the disclosure of the invention. After describing restenosis, the patent continues at page 1₁₆ with a description of intravascular stents. At page 1₂₄ it is observed that the initial data from clinical stent implants shows that they do not significantly reduce the amount of restenosis. It turns then to a discussion of pharmacologic attempts to reduce the amount of restenosis and observes that all of those attempts have dealt with the systemic delivery of drugs via oral or intravascular introduction. It concisely states the objection to systemic administration at page 1₃₃:

“For drug delivery, it has been recognised for a long period of time that pills and injections may not be the best mode of administration. It is very difficult with these types of administration to get constant drug delivery. Through repeated doses, these drugs often cycle through concentration peaks and valleys, resulting in time periods of toxicity and ineffectiveness. Thus, localised drug treatment is warranted.”

[58] The summary of the invention which follows first proposes stents typically for use in the lumen of part of the vascular system and continues (page 2₂₃):

“The prostheses of the invention include at least one drug which will release from the device at a controlled rate to supply the drug where needed without the overkill of systemic delivery. The prostheses include means for fixing the device in the lumen where desired. The prostheses may be completely biodegradable or may be bioabsorbable in whole or in part such that the prostheses will be completely incorporated into the lumen wall as a result of tissue growth, i.e. endothelialisation. Alternatively, the prostheses may be biostable in which case the drug is diffused out from the biostable materials in which it is incorporated.”

One of the possible prostheses designed is a conventional metal stent, and with conventional metal stents it is stated that the invention requires a drug-carrying coating overlying at least a portion of the metal. The introduction to the suitable drugs is given at page 37 as follows:

“The drugs in the prosthesis may be of any type which would be useful in treating the lumen. In order to prevent restenosis in blood vessels, migration and subsequent proliferation of smooth muscle cells must be checked. Platelet aggregation and adhesion can be controlled with antiplatelets and anticoagulants. Growth factor and receptor blockers and antagonists may be used to limit the normal repair response.

The current invention contemplates the usage of any prosthesis which elutes drugs locally to treat a lumen in need of repair. Controlled release, via a bioabsorbable polymer, offers to maintain the drug level within the desired therapeutic range for the duration of the treatment.’

[59] There follows a lengthy discussion of the mechanism of restenosis, and at page 7¹⁹ a passage entitled “Prevention of Restenosis” contains that part of the disclosure about which the debate has concentrated. The passage begins with the statement that in order to prevent restenosis, one must stop the proliferation of smooth muscle cells. It is pointed out that this is a biochemical process which cannot be treated mechanically, and it sets out five hypotheses as to how to stop restenosis biochemically. The first of the five hypotheses is to reduce the adhesion and aggregation of the platelets at the arterial injury site. It is observed that this hypothesis is directly related to the formation of thrombus, and on page 8⁹ two different ways to prevent the adhesion and aggregation of platelets are described. These are the use of an antiplatelet agent and the use of anticoagulants, of which examples are given. The remaining four hypotheses are all, as it is said, closely related. They are said to deal with blocking restenosis during the massive cell migration and replication cycle. In contrast to item 1, they are

said to address the growth factors that are produced from sources other than platelets. The central passage at page 9₁₁ describes these agents as follows:

‘There are several types of drugs that interrupt cell replication. Antimitotics (cytotoxic agents) work directly to prevent cell mitosis (replication), whereas antimetabolites prevent deoxyribose nucleic acid (DNA) synthesis, thus preventing replication. The action of the antimitotics and antimetabolites are so similar, they will be grouped into one category. This category will be known as the anti-replicate drugs.

Anti-replicate drugs include among others: Methotrexate, Azathioprine, Vincristine, VinBlastine, Fluorouracil, Adriamycin and Mutamycin. The target systemic molarity desired with methotrexate is on the order of 10^{-6} M with a range of between 10^{-3} to 10^{-8} Molar. Locally, the molarity of the drug may be highly variable, which is one of the great disadvantages in systemic administration of the drug. When drugs are delivered locally via the prosthesis of the invention, they may be at therapeutic levels at the diseased site while at the lower limits of detectability in the bloodstream. So little drug is required for effective local treatment of a lumen that the drug may not be detectable in blood samples.’

23. In summary therefore, Wolff discloses, amongst other things:
- a) The idea of a drug eluting stent, the purpose of this being to achieve local delivery of the drug;
 - b) The fact that very little drug would be needed because of local delivery;
 - c) That such a stent might be useful to deal with restenosis;
 - d) That the kind of drug which might be used is an “anti-replicate”;
 - e) That “anti-replicate drugs include among others Methotrexate, Azathioprine, Vincristine, VinBlastine, Fluorouracil, Adriamycin and Mutamycin”
24. It is clear that Wolff’s term “anti-proliferative” and the term of the patent “anti-angiogenic” have at least for present purposes, the same meaning. In its unamended form the patent stated:

“... anti angiogenic factors should be understood to include any protein, peptide, chemical or other molecule which acts to inhibit vascular growth.”

Although that passage has been removed by amendment, there is obviously no change in meaning of “anti-angiogenic” for otherwise there would be added subject-matter.

25. Clear confirmation that the two documents are covering the same essential idea by the two terms comes from the fact that the disclosure of the patent as to “anti-angiogenic factors” ranges far and wide. Over a page of the specification (pp.62-715) is devoted to the possibilities. Some are mentioned in more detail than others, starting with AIF (69-18), retinoic acids (619-23), taxol (624-32), suramin (633-39), TIMP and TIMP-2 (639-44) and PA (645-52). It then gives a long list of other possible anti-angiogenic factors:

“A wide variety of anti-angiogenic factors may also be used with the context of the present ~~invention~~ *disclosure*. Representative examples include [there then follows a long list of compounds or in some cases classes of compounds]”

The strikethrough and italics show the amendment, which in no way alters the disclosure or teaching of the patent.

26. Two of the compounds listed in the patent at this point are methotrexate and heparin. Methotrexate is specifically mentioned by Wolff. Heparin has been shown not to be effective – because it is too soluble, but it is clear that the patentee did not know that at the time. Extramustine is also mentioned. This too did not work but again the patentee did not know that at the time. He said both would work and indeed claimed them in original claim 3.

27. So the difference between Wolff and claim 12 is that the patent specifically claims taxol as the factor to be used in a drug eluting stent. The Judge put it this way:

“The difference between the disclosure of Wolff and the inventive concept of the patent in suit is the use of taxol in a drug eluting stent.”

28. As I have said, Mr Waugh attacked that. His point was something to do with the fact that the claim is limited by the word “for” to stents that actually work to prevent restenosis. But that is no different in conception from Wolff. And neither the patent nor Wolff provide any specific detail or evidence that any specific suggestion made by either of them (i.e. of “anti angiogenics” or “proliferatives”) will actually work. They are both saying “these ought to work in principle”.

29. So the problem, obvious or not, boils down to this: Wolff says use an antiproliferative (either an anti-mitotic or an antimetabolite) and gives a wide variety of examples. The patentee originally said use an anti-angiogenic and gave a wide variety of examples. But the patentee in his examples specifically mentioned taxol, whereas Wolff did not. Mr Thorley put the problem this way:

“What it comes down to, my Lords, both patents are teaching that anti-mitotics are good because of their anti-mitotic properties. Where in law does that get us to? Can they

have a patent because they have said taxol is the particular anti-mitotic that does you good because Wolff did not mention it?

30. I think the answer is no. Wolff invites the skilled addressee to consider anti-mitotics as a class. One of those which would naturally occur to the oncologist/cardiologist team is taxol. The team would not know whether in fact taxol would have any better prospect of working than another anti mitotic, whether expressly mentioned by Wolff or not, but that does not matter.
31. The reason it does not matter is because in substance all the patentee has done different from Wolff is to name taxol as a suitable drug along with many others. The fact that now, by amendment, he has reduced his claimed monopoly to just using taxol is irrelevant here. A skilled reader is invited by Wolff to consider “other” anti-replicate drugs. Just to name one “other” anti-replicate which, on the information given in the patent, is no more and no less likely to be found to work in practice is not to make an invention.
32. Things would be different, of course, if the patentee had disclosed that in some way “taxol” was different, or better, or one of only a few anti-proliferatives that would work. His contribution to human knowledge would then be of value. He would have made and disclosed a valuable selection from the range of possible anti-mitotics. As things stand, however, the skilled team would, having read the patent, really know no more than it would having read Wolff.
33. Mr Waugh made a late attempt to suggest that indeed more was disclosed. He pointed to the passage in the patent about CAM assays. This forms example 2. The example is not of a drug eluting stent at all. It is put forward just as a test for anti-angiogenic activity generally. The heading is: “Analysis of various agents for anti-angiogenic activity.” The tests reported show that the application of taxol (not in any way eluted from a plastic, just taxol particles on a methylcellulose disc) to fertilised chicken embryos inhibited angiogenesis.
34. It is true that a little more than that is disclosed at p.19₂₋₁₄:

“Taxol-treated avascular zones already revealed also revealed an abundance of cells arrested in mitosis in all three germ layers of the CAM; this was unique to taxol since no previous study has 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 prevent further blood vessel growth in the treated area. Therefore, even though agents are anti-angiogenic, there are many points in which the angiogenesis process may be targeted.

.... Also we observed the revascularization process into the avascular zone previously described. 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 revascularise for at least 7 days after application implying a more potent long term effect.

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.

35. So I think there is nothing in Mr Waugh's late attempt to get out of the patent some special disclosure about taxol being specially suitable. I add this: this point only emerged in the course of his reply speech. There was no foundation for it in the evidence or argument below, which is why the Judge never dealt with it. I do not regard the point as open since it could well have involved questions of evidence.
36. Mr Waugh advanced a number of arguments as to why picking on taxol was non-obvious. I deal with each briefly bearing in mind in respect of some that Mr Waugh was really asking us to trawl through the evidence just to take a different view from the Judge – a course deprecated by *Biogen*.
37. First, and potentially the most significant, is that the skilled team having thought of taxol, would reject it as potentially too dangerous. This of course concedes that the skilled team would first consider taxol amongst all the possible anti angiogenics. But if the point were right, then it would be fair to regard taxol as a non-obvious choice. The Judge rightly so said at [65]:

“if the skilled man would reject taxol *a priori* even from a test, then the position (i.e. obviousness) would be otherwise”

38. It was this point that formed a major part of the defence of the patent's validity in the evidence before trial. But following cross-examination and assessment of all the evidence it failed. The Judge dealt with this in detail at [68]-[81]. It is not appropriate or necessary to go into this in detail. Mr Waugh did not and could not suggest the Judge had gone wrong in principle on the facts.
39. Given that position, what Mr Waugh endeavoured to do was to say that the Judge had wrongly applied an “obvious to try” test. It is necessary to say a little about this. The expression got into the law of obviousness by virtue of the *Johns-Manville* case, [1967] RPC 479. The facts were simple: there was a known process. The patent was for the old process using the new agent. It was held obvious as being “well worth trying out”. Diplock LJ said:

“It is enough that the person versed in the art would assess the likelihood of success as sufficient to warrant actual trial”

40. More recently, in this court I, with the concurrence of Peter Gibson and Scott Baker LJ said:

“Mere possible inclusion of something within a research programme on the basis you will find out more and something might turn up is not enough. If it were otherwise there would be few inventions which were patentable. The only research which would be worthwhile (because of the prospect of

protection) would be in areas totally devoid of prospect. The “obvious to try test really only works where it is more-or-less self evident that what is being tested ought to work”, *St Gobain v Fusion Provida* [2005] EWCA Civ 177.

41. Judge Rich in the US Court of Appeal for the Federal Circuit said (I did not know this when I wrote *St Gobain*) much the same thing in *Tomlinson’s Appn* (1966) 363 F 2d 298 at 931:

“Slight reflection suggests, we think, that there is usually an element of ‘obviousness to try’ in any research endeavour that is not undertaken with complete blindness but rather with some semblance of a chance of success, and that patentability determinations based on that as the test would not only be contrary to statute but result in a marked deterioration of the whole patent system as an incentive to invest in those efforts and attempts which go by the name of ‘research’.”

42. Mr Waugh submitted that was the correct approach and that it was that approach which was also followed in Australia (*Hässle v Alphapharm* (2002) 312 CLR 411), Canada (*Aventis v Apotex* (2005) [2005] FC 1504) and the USA (*Tomlinson and re O’Farell* (1988) 853 F 2d 894 also *per* Judge Rich).

43. I have to say that I do not discern a shift in the position in this country following the 1977 Act as the majority of the Australian High Court thought had happened. It is perhaps noteworthy that currently Australian courts seem to be taking a very pro-patent view of obviousness and that patents are being upheld there which are not upheld elsewhere. The *Hässle* case and the *Viagra* case, *Pfizer v Lilley* (held by the Federal Court of Appeal non-obvious though invalid on other grounds) are perhaps examples of this. Whether, if that is so, it is good for the Australian economy is not my concern.

44. I also take the view that one can overelaborate a discussion of the concept of “obviousness” so that it becomes metaphysical or endowed with unwritten and unwarranted doctrines, sub-doctrines or even sub-sub-doctrines. This can be coupled with a massive citation of authority (the opinions in the 84 printed page, 203 paragraph judgment, in *Hässle* have 307 footnotes, many of which are citations of authority); Diplock LJ warned against this in *Johns Manville* saying:

“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.”

I interpolate to say, he failed there! Continuing:

“Patent law can too easily be bedevilled by linguistics and the citation of a plethora of cases about inventions of different kinds. The correctness of a decision upon an issue of obviousness does not depend upon whether or not the decider has paraphrased the words of the Act in some particular verbal

formula. I doubt whether there is any verbal formula which is appropriate to all classes of claims.”

45. That reminder cannot be repeated too often. The words of the law are simply:

“An invention shall be considered as involving an inventive step, if, having regard to the state of the art, it is not obvious to a person skilled in the art” (Art 56 EPC).

In the end the question is simply “was the invention obvious?” This involves taking into account a number of factors, for instance the attributes and ckg of the skilled man, the difference between what is claimed and the prior art, whether there is a motive provided or hinted by the prior art and so on. Some factors are more important than others. Sometimes commercial success can demonstrate that an idea was a good one. In others “obvious to try” may come into the assessment. But such a formula cannot itself necessarily provide the answer. Of particular importance is of course the nature of the invention itself.

46. Turning back to this case, Mr Waugh criticised the Judge’s reference to “obvious to try.” Mr Waugh submitted that it was far from self-evident that taxol would work – that there was “no sufficient expectation of success to warrant trial” and that it was not “more-or-less self evident that what is being tested ought to work”.

47. I think the criticism is misplaced. What the Judge actually said was:

“[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 must be some motive making such a stent: but a sufficient motive is the testing of such a stent to see if it has potential in the treatment of restenosis. In the present case, therefore, I reject Mr Waugh’s contention that the definite object in view is the treatment or prevention of restenosis. The object in view is the testing of a taxol-loaded stent to see if it is of any use in the treatment or prevention of restenosis: that is all the specification provides.

[65] In my judgment, therefore, in this case obviousness will be established if on balance the evidence shows that the skilled man would consider taxol to be worth testing to see what its properties were. If the skilled man would reject taxol *a priori* even from a test, then the position is otherwise.”

48. Thus this is not an “obvious to try” case of the *Johns Manville* type. What the Judge is saying overall is that taxol would be included, along with other anti- mitotics, in a

list of “other” anti-replicate drugs. And because the patent has not in any way demonstrated that taxol actually works to prevent restenosis, it is obvious in that sense.

49. I think this decision is not only sound, but accords with rational patent law policy. I have already said that the information in the patent actually adds nothing to the knowledge of the skilled man. So the patentee has done nothing by his disclosure to deserve a monopoly. True it is he mentioned taxol as an idea for a drug eluting stent, but the skilled man, upon reading Wolff would naturally think also of taxol along with the other anti-replicates specifically mentioned.
50. One can, of course, postulate a different policy under which a monopoly might make sense. There are old or obvious ideas which take a lot of work, expense and time to develop and turn into something practical and successful. Without the incentive of a monopoly, people may not do that work or spend the time and money. The Fosamax case, *Teva v Gentili* [2003] EWHC 5 (Patent), [2003] EWCA Civ 1545, is an example of an obvious invention which cost lots to bring to market. But patent law provided no protection for all that investment because the basic invention was obvious. The courts’ job is not, however, to uphold any claim to a monopoly for an idea which requires investment and risk to bring to market, only those for ideas which are new, non-obvious and enabled.
51. That brings me to the next point relied upon by Mr Waugh, commercial success. It is of course well settled that commercial success of an embodiment of an idea may demonstrate that it was a good one – particularly if there was a long-felt want. For why, if it were not inventive, was it not done before? The usefulness of commercial success as a tool in deciding a question of obviousness generally depends on being able to isolate what it is that has contributed to success – so it normally has application only to simple inventions such as the “AnyWayUp Cup” considered by Laddie J in *Haberman v. Jackel* [1999] FSR 683. He made a useful list of factors to be considered when commercial success is invoked as a defence to an obviousness attack.
52. Here, however, commercial success is not of a simple invention. The actual practical, safe and effective taxol eluting vascular stent did not spring onto the market once the “invention” was made. On the contrary it was not until 10 years after the priority date that it came on the market at all. Work had to be done not only in establishing all the detail (appropriate polymer carrier, dose, safety and so on) but, and this is important, as to whether that which in principle ought to work, in fact did so. And meanwhile, and in parallel, another rival drug-eluting stent, also thought of in 1992 but based on rapamycin and outside this patent also reached the market and with equivalent success. It is by no means clear that if yet further equivalent development work on other anti-proliferatives had been done that other drug eluting stents would not have had success too. Commercial success is not shown to be the result of just an inventive idea and the Judge was not shown to be wrong when he so held at [85].
53. Next Mr Waugh relied on the “Holy Grail” paper. It was by the respected Prof. Serruys and others and published (in two parts) some two years before the date of the patent. It is entitled “Pharmacological Approaches to the Prevention of Restenosis following Angioplasty (The search for the Holy Grail?)”. Mr Waugh relied on the

very title as indicating that no-one really knew what to do about restenosis – was the search for something at best elusive or at worst non-existent?

54. The paper describes a variety of approaches to the problem. Mr Waugh submitted that one was left with the view that no one knew what to do – a possible variety of avenues of research were indicated at best. The approaches described include the use of heparin (conclusion: “It appears that heparin [which had been delivered systemically, not via an eluting stent] does not affect restenosis rate dramatically”), hirudin, various antiplatelet agents, anti-proliferatives (ACE, Colchicine, PDGF, angiopeptin, cytostatic agents including doxorubicin, cyclosporine, methotrexate).

55. The paper includes discussion of drug-eluting stents and, following a description of a paper by Cox about stents eluting heparin, methotrexate, and a mixture of both, says:

“The results reported so far suggests that there seems to be no role for cytostatic agents in the prevention of restenosis in human coronary vessels”

This, in effect submitted Mr Waugh, is a real turn-off. Why should one suppose that taxol would work given that? And more especially since Wolff includes methotrexate in his list of possible anti-replicates?

56. The trouble with that argument is two-fold. First it proves too much. For even if the skilled reader was given the disclosure of the patent he would be no further forward. The patent gives him no reason to suppose that taxol would be any better. And after all in its unamended form it too put methotrexate forward as a possible anti-angiogenic factor.

57. The second reason for rejecting the argument is that it was not the cgk that cytostatic agents would be of no use – quite the contrary. The Judge found that:

“[54]Notwithstanding this [i.e. the passage I have just quoted], research into anti-proliferatives generally was one class of work that was still being pursued at the priority date. ”

58. I turn to Mr Waugh’s next point, that the very owners of the Wolff patent, Medtronics, did not consider taxol. The Judge considered this at [86-87] and quite properly took it into account when making his overall assessment of obviousness. There is no error of principle shown. Moreover it would seem that the relevant witness, Dr Muller, was particularly concentrating on agents which had been tried in systemic treatment.

59. There were a number of other matters of fact (e.g. that Dr Cumberland did not consider taxol, that Professor Karsch although he considered taxol did not suggest its use on a stent – a point argued by Mr Birss) which were relied upon. I do not propose to go into all of these – they were taken into account by the Judge and he was not shown to be wrong.

60. Overall then, both Wolff and the patent in suit have wide ranging and overlapping disclosures. That of the patent is wider in many respects. Both suggest drug-eluting stents as a way forward for preventing vascular restenosis. Both propose a variety of

drugs for this purpose. The patent specifically mentions taxol but provides nothing to suggest why it would work whereas other anti-angiogenics (including ones it actually mentions) would not. The patentees did not make an invention in specifically proposing taxol as another possible anti-proliferative. Just adding another, self-evident, candidate to a list of things which might be investigated was not enough to make an invention.

Kopia and Katsuda

61. The Judge also held the patent obvious over these two citations. Mr Thorley accepted that his case was as good on one as the other. I shall just consider one of them and have chosen Kopia. The Judge said:

[90] Kopia is a publication made just a month before the priority date of the patent in suit. It is, like the patent, a long document and its subject matter is a general technique for the delivery of therapeutic agents to their required sites of action within the body. The concept of Kopia may be summarised as the provision of a site-specific molecular fragment to which is attached the drug required to be administered. The idea is explained on page 2₈:

“Drugs that prevent or reduce the proliferation of pathological cell types are essential to the treatment and control of various diseases involving undesirable or uncontrolled cell proliferation. But anti-proliferatives, by definition, must be toxic to certain cell types. It is often not feasible to administer these drugs systemically, because the amounts needed to control the diseased cell types may be toxic or deadly to the patient’s normal cells. This difficulty could be circumvented by administering anti-proliferative agents directly to the site of the undesired cell proliferation. A mechanism is also needed for retaining anti-proliferative agents at the disease site, so that they may effectively control the proliferation of undesired cells, while being restrained from migrating and damaging normal cell types.”

At page 2₃₅, the first application for the technique is identified as post-angioplasty restenosis, and the anti-proliferative agents which are proposed for use with the technique of the invention are heparin (page 3₃₁), colchicine (page 4₂₁) and certain other agents (page 5₇). Further on in the document a section entitled “Treatment of Specific Diseases or Pathological Conditions by Direct Delivery of Therapeutically Active Substances” again starts with post-angioplasty reocclusion and restenosis. The disclosure here is rather different in that the compounds of the invention useful for treatment of post-angioplasty restenosis comprise anti-proliferative agents such as heparin, hirudin, colchicine, vinca alkaloids, taxol and derivatives thereof. The construction of a molecule involving colchicine attached to two

lipophilic tails acid-cleavable from the active molecule is then described.

62. So Kopia specifically suggests (amongst other agents) taxol as a candidate for local delivery to prevent restenosis following angioplasty. (It may be noted that neither he nor Katsuda express any anxiety about taxol being too toxic). As in the case of the patent in suit, Kopia gives no information that taxol or any of the other agents he mentions will actually work or satisfy safety requirements.
63. Now Kopia's proposed chemical method of delivery of the agent is very different from elution from a polymer on a stent. But the Judge found and accepted that the latter concept was well-known (see para. 16(g), 17 and 18 above). So the skilled man/team reading Kopia will see that Kopia's agents (which specifically include taxol) could be delivered locally from a stent. Self-evidently what matters is the fact of delivery, not its manner.
64. The Judge accepted that as an argument for obviousness. Mr Waugh's principal attack upon the judgment was about the concept of drug eluting stents not being cgk – a point I have already rejected at para 19. Once that failed, as it has, I cannot see anything in principle erroneous about the Judge's conclusion. There is no *Biogen* error and I need say no more.

The Dutch Decision

65. I should just add a little about the Dutch decision of 3rd May 2006 concerning the parallel Dutch European patent. It is by the highly respected specialist District Court of the Hague in a case between Angiotech and a company called Sahajanand Medical Technologies. Unlike Pumfrey J (and with the benefit of his judgment) the patent was held valid. I understand the decision is under appeal. There is also a pending decision of the same court in a dispute between Conor and Angiotech.
66. The key parts of the Court's reasoning appears to be that "the patent .. teaches most certainly that precisely taxol should be used to prevent restenosis" (para.4.16). The court did not consider it necessary that the patentee should have provided any data to substantiate this (see para. 4.18). And later the court said "it is legitimate to conclude that the selection of taxol from this large group did not produce an expectable optimal effect but rather a precisely surprising effect: contrary to the other medicines proposed by Wolff ... the taxol-stent precisely does have an effect on prevention of restenosis."
67. So the Court took the view that the patent was in effect a patent by selection – that the patentees had selected the one (or at least one) that would work out of a host of possibles. With great respect I do not agree. This is to read the patent with the hindsight knowledge that taxol stents work. That is just what the skilled man would not know, even by reading the patent. As I was at pains to point out above the patent proposes many things and, unamended, many drugs for a drug eluting stent. Just because taxol is discussed rather more than others is no reason to give the skilled man any reason to suppose it is any more likely to work in practice than any other anti-angiogenic. The further discussion of taxol in the patent is simply not relevant to that consideration.

68. The Dutch court also considered Kopia. Here the evidence seems to be different. In particular it does not seem to have been proved, as it was here, that the concept of a drug eluting stent was well known to the skilled man/team. The argument seems to have been based on a combination of Wolff and Kopia. That is a very different sort of argument from that here, based as it is on what the skilled reader, with his cgk, would see from Kopia. That argument was not considered by the Dutch court. I can well understand a rejection of an argument based on combining Wolff and Kopia – neither as such were proved to be common general knowledge and by well-settled rules it would not be legitimate to read them together.

Conclusion

69. In the result I would dismiss this appeal.

Lord Justice Tuckey: I agree.

Lord Justice Mummery: I also agree.