TRANSLATION

JUDGMENT

THE HAGUE DISTRICT COURT

Civil Law Division

Case number 258022 / HA ZA 06-261

Judgment of 17 January 2007

in the case of

the legal entity under foreign law
CONOR MEDSYSTEMS INC.,
established in Delaware, United States of America,
claimant in the main action defendant in the cross-action,
attorney-of-record mr. P.J.M. von Schmidt auf Altenstadt,
attorney-at-law mr. P.A.M. Hendrick and B.J. Berghuis van Woortman in Amsterdam,

versus

1. the legal entity under foreign law
ANGIOTECH PHARMACEUTICALS INC,
established in Vancouver, Canada,
defendant in the main action,
claimant in the cross-action,
attorney-of-record: mr. H.J.A. Knijff,
attorney-at-law: mr. R.E.P. de Ranitz in The Hague,
2. the legal entity under foreign law
THE UNIVERSITY OF BRITISH COLUMBIA,
established in Vancouver, British Columbia, Canada,
defendant in the main action,
attorney-of-record: mr. H.J.A. Knijff,
attorneys-at-law mr. P.J.M. Steinhauser and O.P. Swens in Amsterdam
3. the legal entity under foreign law
BOSTON SCIENTIFIC CORPORATION,
established in Natick, Massachusetts, United States of America,
party joining the proceedings in the cross-action,
attorney-of-record: mr. H.J.A. Knijff,
attorney-at-law: mr. R.E. Ebbink in Amsterdam.

The parties will be called Conor on the one hand and Angiotech and BSC respectively – together with The University of British Columbia – Angiotech et al..

1. **The procedure**

1.1 The course of the proceedings appears from:
- the interlocutory judgment of 14 June 2006 and the documents listed in it,
- the cross-appeal for inadmissibility, as also motion contesting jurisdiction and statement of reply in the cross-action,
- the brief submitting "Efficiency Aanwijzing" on the part of Angiotech et al.,
- the statement of reply in the jurisdiction interim action, as also brief of reply to the inadmissibility defense, in the cross-action,
- the brief submitting exhibits (58 to 68) of Conor,
- the brief submitting exhibits (30A to 99, including 32 B sent afterwards) of Angiotech et al.,
- the pleading notes of all the parties used at the session of 27 October 2006.

1.2. The judgment was set on this day.

2. The facts

In the main action and in the cross-action

2.1 Angiotech Pharmaceuticals Inc. is active in the field of drug-eluting medical devices and biomaterial. Boston Scientific Corporation is active in the field of medical devices. The companies cooperate in the field of paclitaxel-eluting stents. Angiotech Pharmaceuticals Inc. is the owner together with the University of British Columbia (hereinafter UBC) of European patent 0706376 (hereinafter the (Hunter) patent or EP 376). Boston Scientific Corporation is the licensee in the field of the cardiovascular medicine under EP 376.

2.2 EP 376 was granted on 25 June 1997 following an application of 19 July 1994 for anti-angiogenic compositions and methods of use and claims priority of the American patent application US 94536 which was filed on 19 July 1993. The following countries have been designated: Austria, Belgium, Switzerland, Germany, Denmark, Spain, France, Great Britain, Greece, Ireland, Italy, Liechtenstein, Luxemburg, Monaco, the Netherlands, Portugal and Sweden. The patent was validated in all these countries.

2.3 The claims of EP 376 as granted on 25 June 1997 read – as far as relevant to the present case – in the authentic English language as follows:

> 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.
> 2. A stent according to claim 1 wherein said anti-angiogenic factor is a chemotherapeutic agent.
> 3. A stent according to claim 1 wherein said anti-angiogenic factor is selected from the group consisting of estramustine and methotrexate.
> 4. A stent acccording to claim 1 wherein said anti-angiogenic factor is taxol, or an analogue or derivative thereof.
> 5. A stent according to any one of claims 1 to 4 wherein said polymeric carrier comprises poly (caprolactone).
> 6. A stent according to any one of claims 1 to 4 wherein said polymeric carrier comprises poly (lactic acid).
> 7. A stent according to any one of claims 1 to 4 wherein said polymeric carrier comprises

poly (ethylenevinyl acetate).
8. A stent according to any one of claims 1 to 4 wherein said polymeric carrier comprises a copolymer of poly caprolactone and poly lactic acid.
9. A stent according to any one of claims 1 to 8 wherein said stent is a vascular stent.
…
14. A stent according to any one of Claims 1 to 8 for treating narrowing of a body passageway.
15. A stent according to Claim 14 for treating or preventing recurrent stenosis.
16. Use of a composition comprising an anti-angiogenic factor for the manufacture of a medicament for treating arthritis.
17. Use according to Claim 16 wherein said anti-angiogenic factor is taxol, or an analogue or derivative thereof.
…
25. Use of a composition comprising an anti-angiogenic factor and a polymeric carrier for coating a stent according to anyone of claims 1-15.
26. Use of taxol, or an analogue or derivative thereof for the manufacture of a medicament for anti-angiogenesis.

The patent originally counted 29 claims.

2.4 To the patent initially an opposition was filed by (1) Schering AG, (2) Focal Inc., (3) Inflow Dynamics (this opposition was canceled afterwards), (4) STS Biopolymers Inc. (this opposition was also cancelled afterwards) and (5) Biocompatibles (later Abbott Vascular Devices Limited). By decision of 11 August 2000 the Opposition Division of the European Patent Office (EPO) revoked the patent under Art. 102 (1) EPC.

2.5 From this decision an appeal was lodged on 5 September 2000. In said proceedings a new main request was filed. Seen the fact that the product claims in the new main request had not been examined in the opposition proceedings by the Opposition Division and did not serve as ground for the decision to revoke the patent, the Technical Board of Appeal used its power under Art. 111(1) European Patent Convention (EPC) to refer the case back to the Opposition Division for further examination.

2.6 On 24 January 2005 after a full formal hearing was held attended by the remaining opponents the Opposition Division decided orally that the claims of the (amended) auxiliary request met all conditions of the EPO. The written decision of the Opposition Division with the content of the oral decision of 24 January 2005 was issued on 19 April 2005.

2.7 The claims of EP 376 presently read as follows:

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 antiangiogenic factor is taxol, or an analogue or derivative thereof.
2. A stent according to claim 1, wherein said polymeric carrier comprises poly (caprolactone).
3. A stent according to claim 1, wherein said polymeric carrier comprises poly (lactic acid).
4. A stent according to claim 1, wherein said polymeric carrier comprises poly (ethylenevinyl acetate).
5. A stent according to claim 1, wherein said polymeric carrier comprises a copolymer of poly caprolactone and poly lactic acid.
6. A stent according to any one of claims 1 to 5 wherein said stent is a vascular stent.

7. A stent according to any one of claims 1 to 5 wherein said stent is a biliary stent.
8. A stent according to any one of claims 1 to 5 wherein said stent is a urethral stent.
9. A stent according to any one of claims 1 to 5 wherein said stent is a esophageal stent.
10. A stent according to any one of claims 1 to 5 wherein said stent is a tracheal/bronchial 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.

The original claims 2 to 4 and 16 to 29 have been deleted. A translation into Dutch or a printed version of the new claims has not yet become available.

2.8 None of the opponents has lodged an appeal from this decision of the Opposition Division of the EPO. The patentees did not lodge an appeal either. Conor and Sahajanand Medical Technologies Pvt. Ltd (hereinafter: Sahajanand) nevertheless forwarded a letter including intervention/appeal to the EPO on 28 April and 17 June 2005 respectively.

2.9 Conor is a company established in the United States of America specializing in the technology and design of coronary stents from which drugs can be eluted. It produces among other things drug-eluting stents under the names CoStar and Medstent, which contain as drug paclitaxel, the generic denomination of taxol. At the request of and sponsored by Conor Prof. dr. P.W.J.C. Serruys contributed in 2004/2005 to clinical trials for these stents, called Pisces, Scepter and Eurostar, said trials having been carried out (partly) at the Erasmus University in Rotterdam.

2.10 On 18 November 2005 the Technical Board of Appeal of the EPO handling the case forwarded a preliminary opinion to Conor and Sahajanand involving, to put it briefly, that their intervention/appeal was not admissible with reference to articles 105 and 107 EPC, as well as case-law of the Enlarged Board of Appeal of the EPO (G3/04, G4/91 and in particular G1/94). As reason it was indicated in this that no opposition proceedings were pending anymore (for none of the parties to the opposition had lodged an appeal) when Conor and Sahajanand tried to intervene and lodge an appeal respectively.

2.11 In a press-release dated 17 February 2006 of Conor inter alia the following is stated:

Conor Medsystems,Inc., (Nasdaq: CONR), a pioneer in next generation drug-eluting stents, today announced that it received Conformite Europeen (CE) Mark approval for its Co-Star(TM) cobalt chromium paclitaxel-eluting stent for the treatment of coronary artery disease. CE Mark approval enables Conor Medsystems to commercialize its CoStar stent in the European Union and other countries accepting CE Mark. Beginning immediately, Conor's CoStar stent will be marketed and distributed in these markets by Biotronik AG, a leading manufacturer and global distributor of devices in the area of interventional cardiology.
(…)
In contrast to conventional surface-coated stents, Conor's CoStar cobalt chromium paclitaxel-eluting coronary stent has been specifically designed for vascular drug delivery. The CoStar stent differs from conventional surface-coated drug-eluting stents as it is not coated. Instead, Conor's stent incorporates hundreds of small holes, each acting as a reservoir into which drug-polymer compositions can be loaded. In addition, the CoStar stent uses bioresorbable polymers that are absorbed by the body after the drug is released, leaving no permanent residual polymers or drug at the target site.
(…)

"With more than 800,000 angioplasty procedures performed each year in Europe and the market growing at a rate of almost 10 percent annually, there is tremendous commercial potential for Conor's CoStar stent," said Marlou Janssen, Vice President, Sales and Marketing of Biotronik Vascular Intervention, Biotronik AG. "We are pleased to begin marketing and distribution of Conor's pioneering vascular drug delivery technology."

2.12 The English High Court invalidated the English part of EP 376 by judgment of 24 February 2006 on the ground of its not being inventive (judgment of Pumfrey J, Case No: HC05C00376, Conor v. Angiotech – UBC, see website www.hmcourts-service.gov.uk). An appeal has been lodged from this decision.

2.13 This court ruled by judgment of 3 May 2006 (case number/docket number 258022 / HA ZA 06-261, Angiotech v. Sahajanand, to be found at http://www.boek9.nl/default.aspx?id=2010) that claims 6 and 12 of EP 376 are valid and that they are infringed by Sahajanand with the Infinnium stent.

3 The dispute

3.1 In the main action Conor claims (after also having cancelled its conditional claim initially filed by letter of 14 July 2006) that the court will invalidate the Dutch part of the patent, costs *de iure*. To that end it alleges that the patent lacks an inventive step seen the prior art submitted by Conor (and before the EPO and by Sahajanand), it is insufficient and also extends beyond the content of the application as filed. Angiotech et al. plead a reasoned defense.

3.2 Angiotech and BSC initially claimed in the cross-action (summarizing) a declaratory judgment that Conor infringes directly or indirectly claims 6 and 12 of EP 376 in the Netherlands and in the other designated countries, as well as an injunction (both conditionally and in the case in chief) not to infringe said claims in the Netherlands and in any of the other designated countries, with additional claims, including a moratorium of three years by reason of use of research data unlawfully obtained in the Netherlands for the sake of the application for a CE marking, with damages to be determined by the court and/or account of profit and with costs. By statement/brief of 2 August 2006 Angiotech and BSC restricted their claims in the cross-action to the Netherlands. By fax of 10 August 2006 the attorney-of-record of Angiotech and BSC also announced a restriction to the Netherlands of the conditional claim, but upon oral pleading Angiotech and BSC stated to continue to claim the provisional measure with cross-border effect, which Conor objected to.

3.3 Angiotech and BSC found these claims (summarizing) on the allegation that Conor infringes the patent, because with the CoStar stent and the Medstent clinical trials were and are carried out by a company, called Cardialysis, established in Rotterdam, and/or in the laboratory of Prof. Patrick Serruys in Rotterdam and that for this purpose it imported in any case several stents into the Netherlands, whereas moreover there is a threat of infringement inter alia because a CE marking has been granted to Conor, it expressed the wish to come on the market in Europe with the CoStar stent and the Medstent and the stents are actually on the market in the Netherlands, available through the subsidiary Conor Ireland and the distributor Biotronik respectively.

3.4 Conor pleads a reasoned defense, alleging that there is no infringement, because on the one hand the research of Serruys would be covered by the research exemption or by the

European “Bolar-exemption” of Article 10(6) of Directive 2001/83 EC, amended by Directive 2004/27/EC, there is no threat of infringing acts in the Netherlands and moreover its stent would not fall within the scope of protection of the patent, whereas on the other hand the patent can be considered to be invalid.

4 The examination

In the main action

Validity

4.1 The District Court assumes that the technology at hand is sufficiently known to the reader of this judgment. As far as necessary reference is made to the preliminary remarks in jur.gr. 4.2-4.6 of the judgment of 3 May 2006 in the Angiotech/Sahajanand case.

Added Subject-Matter

4.2 Conor alleges that claim 4 constitutes added matter, because one cannot derive from the original documents the use in a general sense of poly(ethylene-vinyl acetate) as polymeric carrier, but only poly(ethylene-vinyl acetate) and copolymers of ethylene-vinyl acetate, but both always cross-linked with 40% vinyl acetate. The court considers that the argument of Conor is founded on an incorrect reading of the text-parts concerned in the priority document and in the original application. EVA copolymers are, after all, also plainly listed without the addition of a specific cross-link rate, in the (priority) application (priority application US 94536 p. 11, l. 20 and original application p. 14, l. 21-22) *”Representative examples of non-degradable polymers include EVA copolymers, (…)”* Poly(ethylene-vinyl acetate) which is also abbreviated as EVA is a copolymer of two different monomers, i.e. ethylene ($H_2C=CH_2$) monomers and vinyl acetate ($H_2C=CHOCOCH_3$) monomers. The mere fact that some lines below EVA is also recommended if it has been cross-linked with once more with vinyl acetate (40%), does not entail that EVA as such was not sufficiently clearly disclosed as possible polymeric carrier. And so there is no added matter to claim 4 as alleged by Conor.

4.3 As to claim 12 Conor alleged that it cannot be concluded from the original application that restenosis can be prevented, and so the subject-matter of said claim would be inadmissible. The court considers that the prevention of restenosis is most definitely mentioned in the application (and in the priority document US 94536), see pa. 26, l. 7-11 (p. 22, l. 5-9 of US 94536):

> *Briefly, stents may be placed in a wide array of blood vessels, both arteries and veins, <u>to prevent recurrent stenosis at the site of failed angioplasties</u>, to treat narrowings that would likely fail if treated with angioplasty, and to treat post surgical narrowings (e.g., dialysis graft stenosis)*
> .

The light which Conor sees between prevention of restenosis in general and after an angioplasty intervention in particular the court cannot see and has been made insufficiently understandable. The same goes for the difference alleged by Conor between the word “prevent” of the text above and “treat and prevent” of claim 12, taking into account that it appears from the entire description (see e.g. the first

paragraph on “Technical Field”) in both the priority document and the application that it concerns the treatment of angiogenesis-dependent disorders, including therefore restenosis. In the following (as to the inventive step this arguments returns again) it should therefore be assumed that it is sufficiently clear to the average skilled person that the patent (also) relates to prevention (and treatment) of restenosis.

Novelty

4.4 In its intervention with the EPO Conor took the stand that the patent lacked novelty. In the documents of these proceedings it did not develop any argumentation in this respect. The mere reference in no. 29 of the writ of summons to said intervention and the statement that it maintains the allegations thereof and that they should be considered to be inserted by reference, does not suffice to allow it to be characterized as a sufficiently specific claim of non-novelty. In this it is also important that in no. 32 of its writ of summons where it lists the grounds of invalidity Conor omits to submit a lack of novelty, and so Angiotech et al. did not at all discuss this argument in their documents and reasonably did not have to discuss it either. Thus the patent can be considered novel.

Inventive Step

4.5 Furthermore Conor challenged the inventive step of the patent. On this the following is considered.

4.6 According to the patent (to which text-part the Opposition Division of the EPO also refers in its decision mentioned above in 2.6) the following problem is the basis:

> *The major problem with stents, however, is that they do not prevent ingrowth of tumor 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.* (p. 3, l. 17-2 patent).

The patent suggests, according to claims 1, 6 and 12 as presently maintained, to put it briefly, the use of taxol as drug for a drug-eluting stent known as such (for instance from Wolff (WO 91/12779) published on 5 September 1991, D30, Exh. 25 Conor). According to the patent the invention therefore lies in the use of specifically the taxol-stent, which allegedly solves the problem of recurrent ingrowth of body material.

4.7 The court can follow Conor in its pleadings to the extent that the claims of the patent regard a taxol stent to prevent obstructions as a result of ingrowth by reason of tumor/cancer tissue, which after all, claim 1 of the patent not restricted on this point, also regards. Conor alleged with substantiation that neither the patent nor the original documents teach in any manner, or furnish any experimental data, that and why precisely the taxol-stent would have any advantageous effect as chemo therapeuticum upon the closing off of a body-passageway as a result of ingrowth of tumor/cancer tissue. According to Conor there is not even presently any pointer that “*taxol is a better*

chemo therapeuticum for use on a (anticancer, DC) stent than other chemotherapeutica" (oral pleading notes Conor no. 7.13). Angiotech et al. did not refute this with (sufficient) reasons.

4.8 Since it should be assumed that taxol does not have any unexpected (advantageous) effect to prevent obstructions as a result of ingrowth by tumor/cancer tissue, whereas already above it was considered that as such a drug-eluting stent was known and just as much the anti-tumor activity of taxol, it cannot be assumed without any additional information, which lacks, that the mere sum of these features known as such presents a combination effect or synergetic effect. In this it is also important that the use of stents in obstructions of body-passageways by tumors was also already known, witness p. 3, l. 14-15 of the patent:

> *"One device, the stent, has been developed in order to hold open passageways which have been blocked by tumors."*

Even the use of a stent which elutes a chemo therapeuticum upon ingrowth of tumor tissue was already known on the priority date, as described in D82 (D.E. Fleischer and K. Bull-Henry, Gastrointestinal Endoscopy Volume 38, no. 4, 1992, p. 494-3496, '*A New coated self-expanding metal stent for malignant esophageal strictures*'):

> *"Therefore, it seemed relevant to develop a coated stent which would prevent tumor ingrowth, allow removal , and possibly be impregnated with an active pharmacologic agent"* (p. 494, column 1)
> *"An exciting potential of the coating is that it may serve as a carrier into whose interstices an active pharmacologic agent could be placed. A coronary artery stent with a slow release of heparin has previously been conceived (personal communication) and it is possible that for gastrointestinal disea ses the coating could be impregnated with a chemotherapeutic or antibiotic drug."*(p. 496, last paragraph)

The article is clearly focused on obstrictions by tumors, as may already appear from the title and from several text-parts of the article (including the first cited one above).

4.9 Thus claim 1 is a combination of elements which are each known as such to the extent that it regards the treatment of obstrictions by tumors: (i) a stent, (ii) which elutes drugs and (iii) taxol. Without there being any (surprising) synergetic effect such a combination does not produce any inventive step under settled case-law (see T 144/85, T 387/87, T 410/91 and T 363/94). Claim 1 is not inventive for this reason and therefore it should be considered invalid. The allegation that taxol-stents most definitely present such a surprising or advantageous combination effect for the treatment of restenosis, as to be considered below, does not alter this conclusion. This could entail partial invalidity, but claim 1 as it presently reads, cannot be maintained.

4.10 As appears from the pleading notes of Angiotech et al. (more specifically the pleading notes of mr. De Ranitz, who took the pleading on the validity of the Hunter patent upon him on behalf of Angiotech et al.) they also assumed, by the way, that the invention of the patent lies in use upon specific restenosis and not so much upon tumor ingrowth. See for instance no. 5:

"While other researchers were working on different approaches of the restenosis problem, Dr. Hunter and his colleagues used a different line of approach – founded on the study of angiogenesis."

and nos 21, 22 and 23 (read in conjunction):

"<u>The problem to be solved</u>
21. As discussed above the problem which a solution has been looked for for quite some time, was the prevention or treatment of recurrent stenosis. Towards 1993 hundreds of researchers everywhere in the world were busy with different approaches to solve the problem.

<u>The solution to the problem was not obvious</u>
22. The Hunte patent solves the problem with the surprising – and revolutionary – solution of the taxol stent. Contrary to the rest of the field which focused on inhibition of smooth muscle cells or anti-platelet treatments, anti-coagulation treatments or atherectomy aids, Dr. Hunter and his colleagues studied the problem on the basis of insights acquired with their study of angiogenesis.

23. Towards 1993, the direction in which taxol was used for treatment or prevention of restenosis had not been disclosed anywhere (…)."

4.11 Next the question should be answered to what extent the patent can be considered inventive (and can be maintained furthermore) according to one or more of the sub-claims. The court puts a priori that the debate of the parties did not focus on this question, and so – also to avoid any surprise decisions – that a further exchange of briefs is called for. Although in particular the validity of claims 6 and 12 has been discussed, the claims in-between were not actually included in the debate. Nor was for instance amendment of claim 1 discussed, in such a manner that it would regard the treatment of non-tumor-related disorders. The parties did not take into account either that not sooner than in claim 12 the use in restenosis can be found, which is considered crucial to the inventive step, in the text-parts of the pleading notes of Angiotech et al. cited above. Of its own motion the court considers that the parties should discuss in their briefs the question of whether claim 6 can be considered just as much focused on prevention of (re)stenosis or that it should be considered to regard also the obstruction of a vessel by tumor-ingrowth.

4.12 Whatever may be the case, claim 12 is restricted to use in restenosis and Angiotech et al. also pleaded infringement of said claim. As far as partial validity of claim 1 or retreat to sub-claim 12 can be assumed, the court considers in respect of validity of claim 12 as follows.

Inventive Step/Validity Claim 12

4.13 Conor argued that the patent does not regard prevention of restenosis as described in claim 12, because in the description of the patent (as originally granted) restenosis as such was not specifically mentioned. This is not correct. As already considered above in respect of added matter, prevention of restenosis is most definitely mentioned in the

patent, see p. 12, l. 33-38 (said passage being almost identically found in the application and in the priority document, see above in jur.gr. 4.3):

> *Within another embodiment of the invention, 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).*

And so it is sufficiently obvious to the average skilled person that the invention of the patent (also) regards prevention of restenosis.

4.14 In line with the argument stated above concerning use upon tumor-ingrowth Conor argued that neither the patent nor the original documents teach in any manner, or provide any experimental data, that and why precisely the taxol-stent would solve said problem of restenosis. Although it is said in the patent that taxol has an anti-angiogenic effect (in the so-called CAM assay, see example 2) and furthermore that a stent can be coated with a taxol containing polymer, (the priority document or the original application of) the patent lacks any pointer for the skilled person that it be precisely taxol which produces a favorable effect in preventing restenosis. And so it is incorrect to claim as an invention the finding of taxol for a drug-eluting stent which prevents restenosis. This is not the contribution which the patent made to the state of the art, still according to Conor.

4.15 This defense is also left aside. Contrary to that argued by Conor the patent (as well as the original application and the priority document) teaches most certainly that precisely taxol should be used to prevent restenosis. This results sufficiently clear from claims 4, 15, 17, 26 and 28 of the patent originally granted (see jur.gr. 2.3), each individually but more so seen in interrelation. From the priority document the preference for taxol could also clearly be concluded, witness claims 5 and 17 and 26 but in particular 28.The preference for taxol could also already be clearly concluded form the priority document witness claims 5, 17, 25, 26 and 28:

> *5. A composition comprising:*
> *(a) taxol; and*
> *(b) a polymeric carrier.*
>
> *17. A method for eliminating vascular obstructions, comprising inserting a vascular stent into a vascular passageway, the stent having a generally tubular structure, the surface of said structure being coated with a composition according to claims 1-12, such that said vascular obstruction is eliminated.*
>
> *25. A method for inhibiting angiogenesis in patients with non-tumorgenic, angiogenesis-dependent diseases, comprising administering a therapeutically effective amount of a composition comprising taxol to a patient with a non-tumorgenic, angiogenesis-dependent disease, such that the formation of*

new blood vessels is inhibited.

26. A method for embolizing a blood vessel in a [sic] non-tumorgenic, angiogenesis-dependent diseases, comprising delivering to said vessel a therapeutically
effective amount of a composition comprising taxol, such that said vessel is effectively occluded.

28. A method for eliminating vascular obstructions, comprising inserting a vascular stent into a vascular passageway, the stent having a generally tubular structure, the surface of said structure being coated with a composition comprising taxol, such that said vascular obstruction is effectively eliminated.

In sub-claim 28 which under the common systematic of patent specifications will be considered by the skilled person reading the patent to be a preferred embodiment of the invention, the use of the taxol-stent to prevent (re)stenosis is in fact already described (and very specifically). This is even enhanced by the quote cited above in jur.gr. 4.13 of p. 12, l. 33-38 of the patent (corresponding to p. 22, l. 1-9 of the priority document), read in conjunction with the following text-part (p. 4, l. 6-14 of the patent, corresponding to p. 5, l. 15-28 of the priority document):

A method of angiogenesis inhibition is disclosed, comprising administering a therapeutically effective amount of a composition comprising taxol to a patient with a nontumorigenic angiogenesis-dependent disease, such that the formation of new blood vessels is inhibited. (…)
Methods are disclosed for 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 a composition comprising taxol, such that the passageway is expanded.

The text-part first mentioned cited in 4.13 teaches that with a vascular stent provided with an anti-angiogenic factor, restenosis can be prevented and treated, whereas the latter just cited text-part shows that in non-tumorgenous, but angiogenesis-dependent disorders, a stent provided with taxol should be used. Thus these text-parts jointly teach the use of taxol in a vascular stent to prevent restenosis.

4.16 Moreover in example 2 of the patent taxol scores high in the so-called CAM assay, by which the anti-angiogenic effect in vivo is tested on chicken embryos (better than for instance suramine and anti-invasive factor, see example 2B of the priority document). In this a further pointer is to be found for the skilled person that the patent gave a specific preference for using taxol specifically.

4.17 And so seen the fact that the average skilled person would understand from the patent originally granted (the priority document or the application respectively) that according to the patentee it is advantageous to use taxol (with a polymeric carrier) on a drug-eluting vascular stent to prevent restenosis after an angioplasty intervention, it is not required in the view of the court that experimental data concerning such use of taxol stents in humans and the actual prevention of restenosis be included in the patent to further substantiate this. This would only be otherwise if there be doubt as to whether this advantage is indeed achieved with the taxol stent, which Conor did not allege,

however, or if it would be clear that the patent is in fact founded on speculation. Within this context it is further important that in principle testing of a (drug-eluting) stent in the coronary system of pigs is a (ISO) standard test method (more about this in jur.gr. 4.38). Nor is it relevant that the inventors of the patent apparently did not yet test in practice a taxol stent for prevention of restenosis upon an angioplasty intervention, as appeared in the English proceedings (see jur.gr. 2.12):

> "*28. To this extent, therefore, I conclude that the disclosure is indeed speculative. The reason was provided by Dr Hunter's evidence. At the priority date, the Patentees had neither made nor tested any taxol-eluting stent for the prevention of restenosis in percutaneous transluminal coronary angioplasty. By December 1994, work had been done on the use of coated stents for the purpose of treating cancerous blockages, but the evaluation of the usefulness of stents in prevention of arterial restenosis was just being initiated. A document dated August 1995 reveals that by that date no in vivo studies had been performed, and it appears from the evidence that the first such studies were performed somewhat later than this."*

However, in the view of this court there is no speculation by the patentee, as assumed above by the English court. In fact the patentee sufficiently clearly indicates in the patent that it is advantageous to use taxol (inter alia but also specifically for restenosis) and states as reason for this that taxol (as already indicated in jur.gr. 4.6 above) scores well in the CAM assay to demonstrate its anti-angiogenic effect, bearing in mind that the patentee saw the solution for restenosis in the use of an anti-angiogenic factor. The circumstance that other anti-angiogenic factors are also suggested in the patent (and are also specifically claimed in the original documents) does not alter this. After all, this does not deprive the specific unambiguous choice to use the taxol-stent upon restenosis from its inventive character (see above 4.15 and in particular sub-claim 28 of the priority document). It is sufficient that by applying the teaching of the patent the claimed advantage can be effected, and so use of a taxol stent to prevent restenosis after an angioplasty intervention can be considered to be the contribution to the state of the art ("technical contribution").

4.18 Next the court will verify with the problem-solution method whether use of a taxol stent to prevent restenosis after an angioplasty intervention (this according to claim 12) was obvious, or not, seen the state of the art. According to the problem-solution method the following steps can be distinguished:

(i) determining the closest prior art,

(ii) establishing the objective technical problem to be solved on the basis of the differences between such closest prior art and the alleged invention, and

(iii) considering whether or not the claimed invention, starting from the closest prior art and the objective technical problem, would have been obvious to the skilled person.

(i) Closest prior art

4.19 The parties debated on the question of which document should be considered to be the closest prior art. Like the Opposition Division and Angiotech et al. the court assumes that Wolff (WO 91/12779, published on 5 September 1991, D30) comes closest to the

patent. Wolff suggests use of a drug-eluting stent to prevent restenosis, whereat the drug has been applied to the stent in a polymeric carrier. The only difference with the patent, as far as relevant at present, is that Wolff does not disclose the use of taxol specifically. D3, D4 and D32 are more or less equal to D30 and also disclose a drug-eluting stent. D82 (the Fleischer article cited above in jur.gr. 4.8) is less close to the patent, because this document does not principally deal with a drug-eluting stent but only mentions it casually. Moreover said document does not regard treatment and prevention of restenosis but use upon constrictions by tumors. However, even if Fleischer was taken as starting-point, no explicit disclosure of taxol to be used as drug for a drug-eluting stent for prevention or treatment of restenosis can be found in this, and so this should be considered a significant difference.

(ii) Objective technical problem

4.20 In comparison with Wolff in which taxol is not disclosed, the invention is based on the objective technical problem of finding a drug for a drug-eluting stent to allow prevention of restenosis. The court does not believe it is correct to define the problem as finding an alternative drug, because Wolff does not disclose that the medicines suggested in it (inter alia the anti-replicate medicines methotrexate, azathiprine, vincristine, vinblastine, fluorouracil, adriamycine and mutamycine are specifically mentioned) actually help to prevent restenosis. On the contrary, it has meanwhile become known that the medicines specifically stated by Wolff are not effective in preventing restenosis. However, even if the problem was nevertheless found to be the finding of an alternative for the medicines specifically suggested in Wolff, this would not have altered the opinion to be given below. Fleischer only specifically mentions heparine (see the text-part cited in jur.gr. 4.8), nor does said article make a connection with restenosis, and so the objective technical problem cannot be phrased in any case less comprehensively than in respect of Wolff.

(iii) Was the invention obvious?

4.21 Next the question has to be answered whether the use of taxol to prevent restenosis on a drug-eluting stent was obvious, starting from the closest prior art. The court answers this question in the negative, to which end the following is considered.

4.22 After having found that restenosis must be prevented by inhibiting proliferation (growth) of smooth muscle cells (p. 7, l. 19-20) Wolff mentions some five hypotheses of how to stop restenosis in a biochemical manner and explains this (p. 7, l. 25-p.8, l. 7):

> *1. Reduce the adhesion and aggregation of the platelets at the arterial injury site.*
> *2. Block the expression of the growth factors and their receptors.*
> *3. Develop competitive antagonists of the above growth factors.*
> *4. Interfere with the receptor signaling in the responsive cell.*
> *5. Find a "natural" inhibitor of smooth muscle proliferation.*
> *Item #1 is directly related to the formation of thrombus, a major problem with all types of angioplasty procedures. Items #2, #3, and #4 are closely related. They deal with blocking restenosis during the massive cell migration and replication cycle. Unlike item #1, these items address the growth factors that are produced from sources other than platelets. Item #5 is listed to address the question, why don't the 50-80% of the people who don't restenose, restenose. There may be some type of natural inhibitor that these*

people produce that stops the proliferation of smooth muscle cells.

Next examples are given in Wolff of these five categories of medicines. As to medicines which might be suitable to inhibit cell replication Wolff mentions anti-mitotic medicines which prevent cell mitosis and anti-metabolites which prevent DNA synthesis and ranges them in the group of anti-replicate medicines (p. 9, l. 11-18).

4.23 Conor alleged in the first place that the average skilled person with general technical knowledge of the manual of D20 (Molecular Biology of the cell) and the Merck Index (D82) respectively will already read taxol to be comprised in Wolff, at least will immediately think of it. In fact it can be concluded from D20 that next to colchicine, colcemide, nocadazole, vinblastine and vinchristine, taxol is considered to be an anti-mitotic medicine which binds to microtubuli which come about during mitosis.

4.24 The court considers that D20 does not add anything more or else to Wolff than that taxol is also a possible alternative medicine to apply to the stent. However, for there to be an insufficient level of inventiveness the average skilled person should be induced according to settled case-law to use taxol. The question is not whether the skilled person could use taxol, but whether he would actually do so. This means that with the expectance that it (might) prevent restenosis he would have chosen taxol as a result of the pointers in the state of the art. However, one should take into account in this that the average skilled person may be expected to carry out some (routine) research work to optimize known art, and so a selection from a rather limited group of medicines – assuming that the testing of these medicines as such do not involve any special problems for the skilled person or that there is overcoming a prejudice – may produce insufficient level of inventiveness, even if such selection produces an optimum result.[1]

4.25 However, it cannot be retrieved from Wolff alone, nor combined with D20, why the average skilled person would precisely choose taxol. It is relevant in this that Angiotech et al. alleged without being disputed that the "notion of "anti-replicate" encompasses hundreds of structurally and functionally different compounds having in common only the general function of preventing or hindering of cell replication by diverse modes of action" (statement of reply in the cross-action, no. 77). This is supported by the statement of Prof. I. de Scheerder (Exh. 30 Angiotech et al., nos. 116-118), which - after listing the five different categories which Wolff states – says that Wollf suggests "broad drug categories" which comprise "at least hundreds of agents". Prof. J. Feijen also declares that both Wolff and Kopia (WO-93/11120, D40, Exhibit 35 Conor, to be discussed below) disclose broad categories of drugs with hundreds of opitions (Exh. 31 Angiotech et al., no. 26). In the same line also Prof. J. Verweij: "After reading Wolff, I see that it, like Fleischer, fails to provide any guidance to the reader on how to select any particular agent from a list of categories of agents that encompass hundreds, perhaps thousands of distinct agents". As said before, although one may expect the skilled person to carry out some (routine) research work to optimize the art from Wolff,

[1] To that extent the court differs form the opinion of the English court stated in jur.gr. 2.12 which invalidated the patent for lack of inventive step by reason of a different application of the law. In fact the English court examined – to put it briefly – the question whether the average skilled person would consider to try taxol (see in particular jur.gr. 65 of said decision) and next answered it in the positive. Contrary to the court, the English court did not get to the question of whether there was a reason, or not, to choose precisely taxol from the suggested alternatives of the state of the art.

seen this considerable number of possible anti-replicate substances it would go too far to deny the finding of taxol inventivestep by reason thereof.

4.26 Furthermore it has meanwhile become known that among the multitude of studied substances so far only taxol and rapamycin have been successfully applied to a stent to prevent restenosis, and so 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 and D20/Merck Index for a stent, the taxol-stent precisely does have an effect on prevention of restenosis. The court finds it appropriate to take into account this surprising effect, the full extent of which might not have appeared but afterwards, within the context of the inventive step, since it is undoubtedly a continuation of the advantage the patent does claim, the effect on restenosis. The situation at hand can therefore very well be compared so far with the example of the Guidelines of the EPO, Part C, Annex to Chapter IV, ex. 3.2 (ii), which example is considered to be inventive:

> *(II) the invention consists in selecting particular chemical compounds or compositions (including alloys) from a broad field, such compounds or compositions having unexpected advantages.*
> *Example: In the example of a substituted chemical compound given at (iv) under 3.1 above, the invention again resides in the selection of the substituent radical "R" from the total field of possibilities defined in the prior disclosure. In this case, however, not only does the selection embrace a particular area of the possible field, and result in compounds that can be shown to possess advantageous properties (see IV, 9.11 and VI, 5.3.5) but there are no indications which would lead the person skilled in the art to this particular selection rather than any other in order to achieve the advantageous properties.*(underlining added)

As said before, no indication whatsoever appeared in the art to choose precisely taxol and not one of the other ones from the group of anti-replicate or anti-proliferate medicines.

4.27. Moreover Conor wrongfully assumes that Wolff would disclose the use of specific anti-replicate substances for the stent. The mere reference on p. 7, l. 19-20 of Wolff (see jur.gr. 4.23 above) that proliferation of the smooth muscle cells must be stopped in order to prevent restenosis does not make sufficiently obvious and unambiguous the choice of Wolff, advocated by Conor, for anti-proliferative (anti-replicate respectively, let alone anti-mitotic) medicines. The subsequent text in Wolff precisely gives pointers again to use anti-coagulant medicines and anti-platelet medicines and does not show at all any explicit preference for anti-replicates. Claim 3 of Wolff also claims again precisely the large group of “anti-platelet drugs, anticoagulant drugs, anti-inflammatory drugs, antimetabolite drugs and combinations of said drugs”. All this makes it clear that Wolff states rather broad categories of medicines and only makes several specific suggestions as to which type of medicine to be used, but in fact leaves the actual choice up to the reader. D20 adds at the most to the teaching that taxol is also part of this group of medicines, but does not make the choice of specifically taxol obvious.

4.28 Nor does Kopia (D40), combined with Wolff, specifically suggest use of taxol for the stent. Just like D20 Kopia in fact only adds new possible substances to the large group

of medicines of Wolff. Kopia might stress, more clearly than Wolff does, the use of anti-proliferatives to prevent restenosis (p. 50, l. 13-17), but only mentions taxol as example. Taxol is mentioned next to heparin, hirudine, colchicin and vincal kaloids, but also next to “angiotensin converting enzyme (ACE) inhibitors, angiopeptin, cyclosporin A, calcium blockers, goat-antirabbit platelet derived growth factor antibody, Terbinafine and Trapidil, interferon-gamma and polyanions for binding of cationic growth factors.” (see p. 51, l. 28-34). A specific suggestion to use taxol in particular is not found by the skilled person in Kopia. To the contrary, in said paragraph Kopia focuses in particular on colchicin. Not even mentioning that Kopia concerns local administration through inter alia catheterization (not through stents) of conjugates of the medicines with liposomes or virosomes stated in it, which the patent does not regard, and so it remains to be seen whether the average skilled person would combine with Kopia.

4.29 Nor do the documents mentioned also by Conor in this respect (D21, D81, D90, D53, D10 or D38) induce the skilled person to use precisely taxol. No ‘pointers’ to the taxol stent in relation to the treatment and prevention of restenosis can be derived from this. These documents give in particular information on the anti-proliferative action of taxol, and this even in systemic and not in local administration, and so they do not actually teach more than do D20, the Merck Index or D40, said documents already having been discussed above. Garcia-Martinez (Exh. 19 Conor) only further describes the anti-proliferative action of taxol, in that case on the endothelial cells of heart valves in chickens. In none of these documents a link is established between taxol and the prevention of restenosis. It would be illegitimate hindsight to read this in it as yet.

4.30 Although Broder (D53, D53a and Exh. 20 Conor) who writes about the treatment of cancer, adds anti-angiogenic action to the known anti-proliferative and anti-replicate action of taxol, as well as that this medicine may have an anti-tumor effect in this way, these documents also mention taxol in the same breath as other (new) cytotoxic substances, such as camptothecins and “biologic agents”, allegedly having an anti-angiogenic effect. And so once more it concerns a selection from a group of substances without any distinct pointer to taxol. As already considered above the anti-proliferative effect was only seen by the skilled person on the priority date as one of the roads which may be taken into the direction of a method to treat restenosis. This goes just as much for the anti-angiogenic effect, which can in fact be considered to be a subfield of anti-proliferative effect (save for a rare drug which specifically only inhibits angiogenesis, which taxol cannot). Within this context Conor also referred to two articles by Beranek (Exhibits 2 and 3 Conor). In said articles – to put it briefly – an anti-angiogenic approach of the restenosis problem is suggested. However, these articles also do not at all specifically suggest the use of taxol. Beranek even puts a priori that there is a “panoply of antiangiogenic therapies” and next mentions angiotensine converting enzyme inhibitors. Eventually Beranek seems to be taken in particular with hyperbaric oxygen as medicine after angioplasty intervention. In the first place it is such that taxol is not mentioned in these articles at all. Nor does Beranek make it clear that the other roads for treatment of restenosis described in literature (see Wolff above, in particular jur.gr. 4.27) should presently be abandoned, or that at least the quest should focus in particular on anti-angiogenic substances. Thus it cannot be assumed that on the priority date it was totally obvious that an anti-angiogenic substance would be successful. Information about any anti-angiogenic effect of the substances stated by Broder (including taxol) therefore does not add any actually relevant supplementary information to the anti-proliferative effect of taxol already known. Nor do D30 and D40

provide such information. It is equally not clear that even if the average skilled person had focused almost exclusively on the search for an anti-angiogenic substance, he would have chosen taxol from the multitude of such substances. Apparently Beranek did not do so in any case.

4.31 The same goes for the other publications mentioned by Conor which report on the anticancer effect of taxol (Cheson, Bissery, Rowinsky, Hruban, Chang, Murphy, Antler, Hansen, Gale, Burt, Haskell, Bartoli, Jampel and applications WO-93-09765 and WO-92/12717, Exh. 11-14, 16, 23, 24, 26-33 Conor). After all, in relation to claim 12 what is relevant is not so much the effect of taxol on cancer but a sufficiently clear and specific pointer for the effect of taxol on restenosis.

4.32 Furthermore Conor invokes two articles by Katsuda (Exh. 21 and 22 Conor). In these articles it is stated that next to DMSO (dimethyl sulfoxide) taxol also inhibit proliferation of cultivated arteric smooth muscle cells by stabilizing the mictrotubuli as a result of which the DNA synthesis is inhibited. Katsuda also makes a link to atherosclerosis. However, in the view of the court this all does not provide a sufficiently clear pointer to use taxol presently also in restenosis. Rightly Angiotech et al. pointed out that atherosclerosis is in principle a disorder to be clearly distinguished from restenosis, at least Conor did not make the opposite sufficiently comprehensible. The mere fact that an angioplasty intervention is carried out in the first place in patients suffering from atherosclerosis does not yet imply that the average skilled person would immediately make a link between medicine for this disorder and restenosis, the (undesirable) body response to the trauma caused by the angioplasty intervention in the vessel wall. This is the more conclusive, since the article bluntly assumes that atherosclerosis can be treated by inhibiting proliferation of smooth muscle cells in the vessel wall (both articles open with this finding), whereas this was only described as on the possible methods to deal with restenosis (see jur.gr. 4.27 above). Finally the skilled person will even less readily find a pointer in Katsuda for taxol to be used in a stent for the treatment of restenosis, because Katsuda only describes the use of taxol in vitro, whereas it has precisely appeared that many medicines which are anti-proliferative as such or even more specifically anti-angiogenic are not effective in vivo (see jur.gr. 4.25 and 4.26 above), even let alone that in said publications no link is made with stents. Seen the above the court does not find it correct either to characterize Katsuda as closest prior art. After all, Wolff comes closes to the patent according to claim 12, since Wolff describes both drug-eluting stents and restenosis.

4.33 The publication of Coomber (Exhbit 18 Conor) just as much lacks a sufficiently clear and specific ‘pointer’ as stated above. This article discusses inhibition by taxol of proliferation in the healing process of a wound. However, as already considered above, on the priority date there were still several roads open to prevent and treat restenosis, of which inhibition of proliferation was only one. Moreover Conor did not make it sufficiently comprehensible that the average skilled person would immediately link the antiproliferative effect of taxol on renewed endothelial cell formation after wounding with (anti-angiogenic) effect on restenosis. Finally the average skilled person would also have to take the step from Coomber to understand that this article concerns inhibition *in vitro*, whereas precisely the favorable effect of taxol *in vivo* is relevant.

4.34 The mere fact that taxol might have been (also on the priority date) a rather known anti-proliferative medicine which was in the public eye for that reason, does not effect that

there is a sufficient technically relevant 'pointer' to taxol. This would be different, if in respect of such being known Conor had alleged while stating sufficient reasons and proven – which it has not – that taxol would have been studied without any restriction as the first one or one of the first ones of said group of hundreds of anti-proliferatives/anti-replicates by the skilled person. Nor did this appear sufficiently clear otherwise, bearing in mind in the first place that taxol was not mentioned as example by Wolff, nor by Wolff in his continuation-in-part application, filed five months following the priority date and three years following the submission of D30, was claimed (US application with number 08/171,361, granted patent US 5,545,208, Exh. 21 Angiotech et al.).

4.35 The conclusion in respect of the inventive step reads that the choice of a taxol-stent to treat or prevent restenosis, was not obvious. The problem of the lack of a synergetic effect which was fatal for claim 1, does not play a part in restriction to restenosis. After all, the taxol stent does have a synergetic effect in restenosis, as considered in jur.gr. 4.26 above, because – unexpectedly and contrary to the other medicines suggested in the prior art – taxol does help against restenosis. Moreover the use of taxol specifically in prevention and treatment of restenosis (contrary to cancer) was not specifically disclosed. The court cannot follow Conor in its argumentation (not further substantiated) that the restriction to restenosis in claim 12 could not contribute to patentability, since it would concern an intended purpose of the stent. After all, under settled case-law such features can also produce an inventive step.

4.36 Seen the above the allegation of Angiotech et al. that there be a prejudice to the use of taxol in respect with (inter alia) cardio-toxicity and other reported side-effects of this medicine no longer has to be discussed.

Sufficiency

4.37 Conor claims that the patent (presently to be understood as according to claim 12) is insufficient on two points. The court states a priori that in principle it is up to Conor to allege, and to prove when contested, that the patent does not sufficiently diclose the invention.

4.38 In the first place Conor alleges that the exact meaning of the term "analogue or derivative" of taxol is not clear. Let alone that in fact this boils down to pleading that the claim is insufficiently clear, which under Article 70 Dutch Patent Act is not a ground for invalidation, the court does most definitely find this term sufficiently clear. After all, the point within the context of sufficient disclosure is whether the average skilled person can carry out the invention on the basis of the patent specification and his general knowledge. This is the case, were it only because the medicine taxol was available on the market. Conor did not make it sufficiently comprehensible that the average skilled person would not be able to next make analogues or derivatives from it, or to oversee what this term would imply, respectively. Such comprehensibility also lacks from the allegation of Conor that some derivatives of taxol would not be effective, seeing that if not the CAM assay then at least the ISO standard tests by means of implantation in the coronary system of pigs, to be discussed below, offer the average skilled person sufficient clarity.

4.39 In the second place Conor alleges that the invention is not sufficiently disclosed, because many polymers are mentioned in the patent and it would be an "undue burden"

for the average skilled person to select the right one form this multitude. In the first place the court finds this allegation hard to reconcile with the fact that Conor's stent contains PLGA as copolymer itself, said copolymer precisely been specifically stated in the patent (p. 7, l. 41-42). Furthermore it cannot be undeniably concluded from the statement of Dr. K.A. Robinson (Exhibit 47 Conor) that this copolymer would be completely unfit, which is apparently not the case either, witness Conor's own stent. Apparently said researcher for other reasons made a stent with a taxol/PLGA mixture which was not well received in the coronary system of pigs.

4.40 Furthermore Conor did not sufficiently state to challenge the reasoned contestation by Angiotech et al. that there are routine tests (according to the ISO standard) to study the tolerance of the polymer/taxol mixture *in vivo* (although not yet in humans) by implanting the stent in the coronary system of a pig. Although this will without any doubt involve some work for the average skilled person, the court finds it insufficiently shown by Conor that carrying out such tests in pigs would impose an "undue burden" on such skilled person. Like the Opposition Division of the EPO the court therefore believes that the patent insofar sufficiently discloses the invention..

Conclusion Invalidity

4.41 Claim 1 of the patent lacks inventive step. As regards partially upholding it, the parties will express their further views. At any rate, the Court rules that claim 12 is inventive and also furthermore valid. Whatever the outcome of the debate on partial validity, a retreat by Angiotech to claim 12 will be deemed to be justified. In this respect the following is considered.

4.42 Partial invalidation and amended upholding of a patent is, according to the Netherlands Supreme Court, *only permissible if it is sufficiently clear to the average skilled person who reads both the patent specification and prior art on the priority date, where the limits of the protection run which the patent offers as far as it is valid. This does not only require that an addition to the patent specification may be phrased afterwards, thus drawing said limits with sufficient clarity, but also that it concerns an addition which was already sufficiently obvious to the average skilled person beforehand to independently reach, on the basis of the content of the patent specification in conjunction with the prior art on the priority date, the conclusion that the patent should only have been granted including the restriction comprised in such addition and that for this reason it was valid within the stricter limits to be concluded from this.*

4.43 These criteria phrased by the Supreme Court in its judgment in Spiro/Flamco (NJ 1998, 2) were derived form the legal requirements (see Article 75(1)(a)-(d) DPA) on the one hand, and the legitimate interests of third parties on the other hand, also in respect of the retroactive effect of invalidation. As results from that considered above the criteria founded on the legal requirements have been met as far as claim 12 concerns. Although the court finds an exchange of positions called for on the question of whether partial upholding should be made according to one or more of the claims 2-12 or according to another amendment of claim 1, it can already answer the question of whether the legitimate interests of third parties, in particular from the view of legal certainty, would oppose that the court assumed that the patent could be maintained according to claim 12. The court answers this question in the negative. It was totally clear to the average skilled person that the scope of protection of the patent covered in any case claim 12 since this

is a sub-claim. After all, the drafting of sub-claims has as main, if not only, purpose to anticipate possible invalidity of the main claim and thus prevent the patentee from losing his entire monopoly, if – for instance as a result of prior publications found afterwards – his claim would be too broad. This is clearly known to the average skilled person and so he will also know that upholding according to a dependant sub-claim is called for provided that it meets the legal requirements and in case of invalidity of preceding claims. Under these circumstances it cannot be understood that the legal certainty or any other legitimate interest of third parties would prevent the patent from being partially maintained according to a sub-claim, in this case claim 12.

4.44 Moreover, any other opinion would result into a disproportionate disadvantage for the patentee, who will see his position seriously complicated, also seen the Bogard decision (The Hague Appeal Court, 1 March 2001, knowable from SC 21 February 2003, BIE 2004, 29) and precisely create legal uncertainty by this. According to the system illustrated above third parties will rather easily be able to predict any new scope of the patent, bearing in mind that the patentee knows that by retreat to such a sub-claim the debate on the question of whether his proposal meets the Spiro v. Flamco criteria stated above, is largely simplified. Such certainty has disappeared, if it be assumed that it would also be uncertain in respect of sub-claims which nevertheless meet the legal criteria whether they meet the Spiro v. Flamco criteria, or not.

4.45 A stay of the proceedings pending the opposition/appeal proceedings instituted by Conor and Sahajanand with the EPO is not found opportune for the time being, because it is, if not unlikely, than to say the least it is rather uncertain whether said proceedings will result into examination of the merits seen inter alia the provisional judgment of the EPO and the case-law of the Enlarged Board of Appeal cited in it (in particular G 1/94, see jur.gr. 2.10 above). Furthermore it is likely that a final decision on this will be there as soon as the court will have to render its final judgment in this case.

4.46 Any further decision in the main action will be held over. For reasons of trial economy the court will allow, as far as the law requires, interlocutory appeal from this judgment.

In the cross-action

In the interim action

4.47 The attorney-of-record of Angiotech and BSC announced by fax of 10 August 2006 that not only the principal claim but also the provisional relief claim in the cross-action would be restricted to the Netherlands at oral pleading. To the extent that Angiotech and BSC intended to maintain their provisional relief claim nevertheless with a cross-border effect, this will be contrary to due process.

4.48 Thus the court understands that the raised interim claim does not require any decision anymore.

In the case in chief

4.49 The validity defense pleas in the cross-action do not hold in any case to the extent that they concern claim 12, and so the court reaches the question whether this claim is infringed, at least that a sufficient threat thereof can be assumed.

Admissibility

4.50 As to the counterclaim Conor took the stand that Angiotech and BSC already filed this claim in two previous proceedings before this court instituted by Angiotech and BSC (docket numbers 2005/1318 and 2005/1472), and so it would be contrary to due process if Angiotech and BSC were admitted in their claim. The court finds this defense unfounded, whereat it took the following into account.

4.51 It is a priori that in principle a counterclaim is considered admissible in any proceeding under the accelerated regime in patent matters. For a correct and trial economical handling of a patent case it is in general desirable, after all, that invalidity and infringement can be decided in the same proceedings. Filing a counterclaim to raise the infringement or – subject to the case – the invalidity will therefore not readily violate due process..

4.52 In order to answer the question of whether the infringement counterclaim of Angiotech and BSC would nevertheless be contrary to due process it is useful to sketch the procedural background of this dispute. Angiotech and BSC were the first to start an ordinary procedure on the merits concerning the infringement by serving a writ of summons on 1 February 2005. This case will be pleaded on 8 June 2007 before the court. The second infringement case instituted by Angiotech and BSC would run through the accelerated regime of this court which applies specifically to patent matters, which leave was granted for on 7 February 2005. This decision provided for an oral pleading date on 9 December 2005. However, since Conor did not appear on the first day the case came up in court, 20 April 2005, despite a writ of summons on 10 February 2005 this case was removed from the accelerated regime by the court. Meanwhile Conor started in its turn the present proceedings once more accelerated with the aim of having the patent invalidated. When Angiotech and BSC next requested joining of the ordinary procedure on the merits with the present proceedings Conor opposed this, and next the court decided by interlocutory judgment of 14 June 2006 not to allow joining of the proceedings. Looking at all these circumstances the court cannot understand that Conor may still rightly invoke violation of due process as yet in respect of the infringement counterclaim. After all, if Conor had cooperated in joining the proceedings, or had appeared in the accelerated procedure on the merits initiated by Angiotech and BSC, the problem sketched by it would not have come about. Furthermore it is relevant to this that it did not state any reasons why it did not appear in said proceedings. Moreover a different opinion would entail the irreconcilable outcome that although over half a year sooner they initiated (accelerated) proceedings, Angiotech and BSC would nevertheless get a decision of their claim at a considerably later date by the instigation of Conor. Finally it is important that the court in its interlocutory judgment precisely considered that, since the dispute (both as to infringement and as to invalidity) is presented in these proceedings in its full extent, it could not be understood at the time why the claimed joining would be desirable for reasons of trial economy (jur.gr. 4.2).

4.53 In these circumstances it cannot be assumed either that Angiotech and BSC would not have any interest to be respected by law in their claims in the present proceedings by reason of having their claims already filed earlier.

Infringement

4.54 The court considers that there is a sufficiently serious threat of infringement, whereas the following is considered in support of this. In the first place the allegation of Conor that the Co-Star stent and the Medstent would not fall under the scope of protection of said claim of the patent, is left aside for the following reasons.

Scope of Protection

4.55 Upon examining whether there is (literal) infringement it is a priori that when interpreting the claims of a patent specification, also in the light of the description and drawings, one should identify what according to the skilled person reading this, is essential to the invention the protection of which is claimed – to put it differently: what the inventive thought is underlying the words of these claims – in order to avoid an interpretation exclusively founded on the literal meaning of the wording and therefore possibly too restricted (or needlessly broad) for a reasonable protection for the patentee. However, the court called to interpret the claims of the patent specification will also have to examine whether the results of his examination sufficiently respect legal certainty for third parties. The latter point of view may justify a restrictive interpretation more in line with the wording of the claims in the sense that lack of clarity for the average skilled person who wants to define the limits of the protection offered by the patent, should in principle be to the disadvantage of the patentee (see NethSC 12 November 2004, NJ 2004, 674, Impro v. Liko and NethSC 13 January 1995, NJ 1995, 391 Ciba Geigy v. Oté Optics).

4.56 When applying said criterion it is clear that both the CoStar stent and the Medstent fall under the protection of claim 12. The inventive thought underlying the wording of claim 12 is the use of taxol applied (in a polymer) to a stent in order to prevent restenosis. It is clear that it does not matter to such an invention in which way exactly taxol with the polymer has been applied to the stent. The point is whether "*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*" (patent B1 text, p. 10, l. 51-53). In short, contrary to that argued by Conor, the average skilled person will understand that the taxol/polymer mixture must adhere to the stent to such an extent that it will not dislodge upon inserting or expanding the stent and that is also how he will interpret the term "coated with".

4.57 Moreover, the average skilled person knows from examples a-e of the patent that the term "coated with" has been defined more broadly than the usual sense (B1 text, p. 10, l. 44-50):

> *"Stents may be coated with anti-angiogenic compositions or antiangiogenic factors of2 the present invention using a variety of methods, including for example: (a) by directly affixing to the stent an anti-angiogenic composition (e.g., by either spraying the stent with a polymer/drug film, or by dipping the stent into a polymer/drug solution), (b) by coating the stent*

with a substance such as a hydrogel which will in turn absorb the antiangiogenic composition (or anti-angiogenic factor above), (c) by interweaving anti-angiogenic composition coated thread (or the polymer itself formed into a thread) into the stent structure, (d) by inserting the stent into a sleeve or mesh which is comprised of or coated with an anti-angiogenic composition, or (e) constructing the stent itself with an anti-angiogenic composition."

After all, in particular examples c to e will not immediately be considered to be a way of coating by the average skilled person, as the ones he is used to understand by it. So, also from this he will draw the conclusion that the term "coated with" should not be taken too literally, as this term may be used in normal technical parlance, but in the broader sense indicated above. From this view the average skilled person will acknowledge that a stent like the one of Conor in which the paclitaxel/polymer mixture has been applied in cavities (let alone whether they are through-and-through holes in the stent or only pits), meets the inventive thought of the patent. Moreover the average skilled person will be aware that also upon applying in cavities in any case the sidewalls of such cavities will most certainly have been coated with said mixture and so as such coated in the more general meaning of the word.

4.58 The court fails to understand that this interpretation of the patent would prejudice legal certainty of third parties like Conor. As said before, the third party could, after all, already read in the description of the patent itself what the intention was of the term "coated with" and the examples of "coated with" stated in the description are self-explanatory. On the contrary, the third party cannot read anywhere in the patent that only a stent with an uninterrupted coating would be covered by this, let alone that it was intended to have a stent with a mixture divided over pits or cavities fall outside the protection. This is not any different after reading the text-part which Conor also referred to, i.e. that the mixture would coat the stents "smoothly and evenly, with a uniform distribution of angiogenesis factor" (p. 10, l. 54-55, B1 version patent). After all, the average skilled person will understand that only a preferred embodiment of "coated with" is described here by reason of the use of the word "preferably" in the introduction of the phrase in question. Thus the stents of Conor fall under the patent in a literal sense.

4.59 The court cannot follow Conor in its allegation that PLGA would not be a polymeric carrier in the sense of the patent. After all, this polymer is stated specifically in the patent (see jur.gr. 4.2 above). This opinion is not altered by the mere fact that Boston Scientific's Taxus stent and Johnson & Johnson's Cypher stent have been provided with a more flexible polymer.

Research Exemption

4.60 It has not been sufficiently refuted that Conor imported and delivered stents in the Netherlands for the sake of the Pisces, Scepter and Eurostar trials, which were partly carried out by Serruys (see jur.gr. 2.9). This research sponsored by Conor does not fall under the research exemption. In fact the court finds that it has become insufficiently clear that these trials had a purely scientific purpose and could therefore profit from the legal research exemption. The following is considered in that respect.

4.61 In the first place it is sufficiently clear that the study results were used by Conor to obtain the CE marking (statement J.F. Shanley, Chief Technical Officer of Conor before the Australian court, no. 15, Exh. 48 Conor). Furthermore it is such that Conor on which the duty to state fact and the onus of proof rests, did not state with sufficient reasons that these trials would nevertheless exclusively concern research into an improved stent. It does not appear from the statement of Shanley referred to above (nos. 9, 11 and 15) that these trials were aimed at any improvement. On the contrary, they were intended "*to evaluate our paclitaxel stainless steel stents for safety and performance, measuring the late loss of vessel lumen diameter versus our bare metal stent*". Would the research actually be aimed at improvements, not comparison with a bare metal stent would have been obvious, but rather with an already existing stent coated with paclitaxel and a polymer. Furthermore it is illustrative the following statement of Conor in its SEC Report (Form 10-K, p. 42 of 59, Exh. 11J Angiotech and BSC):

> *We may be unable to demonstrate that our CoStar stent offers any advantages over Johnson & Johnson's CYPHER™ stent or Boston Scientific's TAXUS™ Express2™ stent."*

4.62 And so it concerns pre-marketing research which cannot benefit from the previously mentioned research exemption. This is not any different by the implementation of Directive 2001/83/EC as amended by Directive 2004/27/EC of 31 March 2004, seeing that the implementation time-limit of the latter Directive (30 October 2005, see Article 3) had not yet expired when the trials were held.[2] Article 10(6) of the first Directive presently reads after the latter amendment as follows:

> *6. Conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products*

.

It would go too much against settled case-law on the research exemption in this country to interpret the DPA in conformity with the Directive prior to the date of implementation. The court even leaves aside the question of whether said research by Serruys would fall under the effect of Article 10(6) of the Directive, for being not for a generic medicine but for use of a medicine on a stent.

4.63 Nor did Conor state to wish to take out a license under the patent, as may already appear from its attitude in the present proceedings, and so this purpose cannot be alleged either as justification for having Serruys try the stents.

Threat of Infringing Acts

4.64 Furthermore Conor took the stand that it would not perform any act restricted to the patentee and so there would not be a sufficient threat of infringement to legitimate an injunction. This defense is also left aside, because a sufficient serious threat comes from the following circumstances jointly that with its stents Conor performs or will perform a restricted act in the Netherlands.

[2] No sooner than on 30 November 2006 was the implementation Act adopted, which will become effective on 1 February 2007 (Stb. 2006, 672).

4.65 In the first place it is important that by the delivery for the sake of said trial by Conor in this country the patent rights of Angiotech and BSC have been infringed. Without any sufficiently clear cease-and-desist declaration subjected to fines the threat of further infringement after infringement in the past is in principle sufficiently given. Moreover a CE marking has been granted to Conor for the CoStar stent under which in principle it can also come on the market in the Netherlands, as it also announced on 17 February 2006 (see jur.gr. 2.11). Furthermore it has not been disputed that the stents are produced by Conor and next are available in the Netherlands through its subsidiary Conor Ireland, this under the effect of the CE marking belonging to Conor. It also appears form the internet site of Conor itself that for the Netherlands distribution of the CoStar stent is carried out by Biotronik AG in Switzerland, said company moreover also having a subsidiary in the Netherlands (Biotronik Nederland B.V.). In fact this can be characterized as an invitation to visitors of the site looking for the stent in the Netherlands to purchase it from Biotronik and as such an offering of the stent in the Netherlands. Finally, the instructions for use of the stent have also been provided in Dutch.

Conclusion in the Cross-Action

4.66 Conor's CoStar and Medstent fall within the scope of protection of claim 12 of the patent, whereas the invalidity defenses aimed therat do not hold. Conor's import and delivery for the sake of the trial carried out by Serruys constituted infringement of the patent rights of Angiotech and BSC. Furthermore there is a threat of infringement, and so the declaration and the injunction are allowable as far as claim 12 is concerned. Seeing that the declaration and the injunction can therefore be allowed, it cannot be understood which interest Angiotech and BSC might have in any examination of the infringement according to claim 6, and so the declaration and the injunction will already be dismissed at present to that extent and the final decision on this point in the main action does not have to be waited for.

4.67. What purpose the moratorium of three years also claimed might also serve is not readily clear, but assuming that this should start upon expiry of the patent protection the court considers that it has not become sufficiently clear in the present proceedings that without the results of any infringing acts here in this country (more specifically the trials by Serruys) no CE marking would have been granted. Insufficient is the fact that the trials which Conor used to apply for a CE marking took place in the Netherlands for 20% and apparently were also founded for 20% on infringing acts in the Netherlands. It has not become clear that and why the results concerning the other 80% of the trials which were obtained outside the Netherlands, would not have been sufficient to obtain a CE marking. Nor can it be understood which purpose an injunction not to use the data of the trials in advertising or upon sale might serve, since it is no longer allowed to sell or offer the stents in the Netherlands as a result of the general infringement injunction to be allowed sub 1 and the injunction not to use said data would only concern the Netherlands.

4.68 Furthermore Angiotech and BSC did not allege with sufficient reasons why the injunction should also cover branches or subsidiaries of Conor, which are after all not a party to these present proceedings, or in which way Conor threatens to indirectly infringe the patent, and so all this will be dismissed.

4.69 It has become sufficiently likely that it is possible that Angiotech and BSC incurred some damage as a result of the established patent infringement, which can, however, be assessed on the basis of the profit effect by this by Conor. The claims for damages to be determined by the court is therefore open to allowance. The court further considers – with reference to NethSC 14 April 2000, NJ 2000, 489 – that damages and account of profit cannot accumulate unlimitedly. No more than a sum equaling the highest of the total sums claimed for the account of profit and damages respectively consisting of loss of license fees can be allowed. And so Angiotech and BSCare allowed to choose the highest one of these two items claimed after the damage has been determined. Accumulation of account of profit and any other items of loss (depreciation of patent right and for instance extrajudicial costs) is possible. For an order to give a bank guarantee of EUR 10 million the court does not see any reason, since it has not been made likely that the damage will amount to such a sum.

4.70 The claimed civil fine will be moderated to EUR 10,000.—for each stent or day, at the discretion of Angiotech and BSC. The conditional claim does not come up, because at present an injunction can already be given. To the extent that the conditional claim also concerns cross-border measures, the court does not find Angiotech and BSC admissible in this – as already considered above. The court does not see any reason not to declare the claims enforceable notwithstanding appeal as claimed save for the court declaration.

4.71 Being the party found to be at fault Conor will be ordered to pay the costs of the proceedings. The costs on the part of Angiotech et al. are assessed at the fees of the attorney-of-record to the amount of EUR 1,356.00 (3.0 points x factor 1.0 x rate EUR 452.00).

4.72 For reasons of procedural economy the court will , as far as required by law, also allow interim appeal from this judgment in the cross-action.

5. The Decision

The Court

In the main action:

5.1 provides that the case will be placed on the docket of 18 April 2007 for Angiotech c.s. to submit a written brief relating to what has been considered in par. 4.11;

5.2 defers any further decisions;

In the cross-action:

<u>in the jurisdiction interim action</u>

5.3. determines that in this regard no further decision is necessary

in the case in chief

5.4 declares that Conor directly infringes claim 12 of EP 0 706 376 in the Netherlands, more in particular by selling, marketing and delivering – as well as importing, offering, or keeping in stock for these purposes – its paclitaxel-eluting stents in the Netherlands;

5.5 orders that Conor must stop the direct infringement of claim 12 of EP 0 706 376 in the Netherlands, more in particular by selling, marketing and delivering – as well as importing, offering, or keeping in stock for these purposes – its paclitaxel-eluting stents in the Netherlands;

5.6 condemns Conor to pay to Angiotech and BSC a penalty sum to a total of EURO 10.000 per stent or – to the choice of Angiotech and BSC – for each day that Conor does not fully comply with the aforementioned order;

5.7 condemns Conor to pay to Angiotech and BSC a full compensation of damages, to be established in subsequent proceedings and/or to surrender the profits obtained with or with the aid of the infringing stents;

5.8 condemnts Conor to pay the costs in the cross-action, to this date at the side of Angiotech and BSC estimated at EUR 1.356,00;

5.9 declares this judgment in the cross-action, with the exception of the declaratory judgment, enforceable notwithstanding appeal;

5.10 denies that which was claimed in the cross-action more or differently

In the main action and in the cross-action

5.11 provides that appeal against this judgment may be lodged before the final judgment has been given.

This judgment has been issued by mr. G.R.B. van Peursem, mr. E.F. Brinkman and mr. P.W. van Straalen and declared publicly on 17 January 2007.

[two signatures]