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D E C I S I O N
of 28 October 2002

Case Number: T 0890/00 - 3.3.2

Application Number: 94920360.8

Publication Number: 0706376

IPC: A61K 9/16

Language of the proceedings: EN

Title of invention:
Anti-angiogenic compositions and methods of use

Patentee:
Angiotech Pharmaceuticals, Inc., et al

Opponents:
(I) Schering AG
(II) Focal, Inc.
(III) Inflow Dynamics AG
(IV) STS Biopolymers Inc.
(V) Abbott Vascular Devices Limited

Headword:
Anti-angiogenic compositions/ANGIOTECH PHARMACEUTICALS

Relevant legal provisions:
EPC Art. 123(2), (3); 84; 111(1)

Keyword:
"Remittal to the first instance for further prosecution-
New main request not examined for all EPC requirements"
"Apportionment of costs (no): more appropriate for decision at end of further first instance proceedings"

Decisions cited:
T 0715/95, T 0048/00

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0890/00 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 28 October 2002

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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 11 August 2000 revoking European patent No. 0 706 376 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: U. Oswald
Members: M. Ortega Plaza
C. Rennie-Smith

Summary of facts and submissions

I. European patent No. 0 706 376 based on application No. 94 920 360.8 (published as WO-A-95 030 36) was granted on the basis of 29 claims.

Independent claim 1 as granted 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."

Claims 2 to 15 and 29 as granted related to product claims dependent on claim 1.

Independent claim 16 as granted read as follows:

"16. Use of a composition comprising an anti-angiogenic factor for the manufacture of a medicament for treating arthritis."

Claims 17 to 24 as granted related to dependent use claims.

Independent claim 25 as granted read as follows:

"25. Use of a composition comprising an anti-angiogenic factor and a polymeric carrier for coating a stent according to any one of claims 1-15."

Independent claim 26 as granted read as follows:

"26. Use of taxol, or an analogue or derivative

thereof, for the manufacture of a medicament for anti-angiogenesis."

Claims 27 and 28 as granted read respectively:

"27. Use according to claim 26 wherein said medicament is for treating psoriasis."

"28. Use according to claim 26 wherein said medicament is for treating vascular adhesions."

II. Notices of opposition were filed against the granted patent by five opponents (respondents).

The patent was opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC), lack of inventive step (Article 56 EPC) and because the subject-matter is not susceptible of industrial application (Article 52(4) EPC); Article 100(b) EPC on the grounds of insufficiency of disclosure and Article 100(c) EPC on the grounds of unallowable extension beyond the content of the application as filed.

The following documents *inter alia* were cited during the proceedings:

D39: Review "Inhibitors of angiogenesis" M. A. Moses and R. Langer, BIO/TECHNOLOGY, July 1991, vol. 9, 630-634.

D40: WO-A-9 311 120

D47: US-A-5 092 885

III. By its decision of 11 August 2000, the Opposition Division revoked the patent under Article 102(1) EPC.

The Opposition Division took the view that the use claim 22 of the main request (which corresponded to claim 26 as granted), claim 22 of auxiliary requests 1 to 3, claim 23 of auxiliary request 4 and claim 21 for auxiliary request 5 respectively, all failed to meet the requirements of the EPC. In particular, claim 22 of the main request was considered to lack novelty *vis-à-vis* the contents of D40.

The Opposition Division concluded that document D40 anticipated the subject-matter of claim 22 of the main request, as it disclosed that some antiproliferative compounds, among others taxol, are useful for the treatment of post-angioplasty restenosis and in view of the fact that restenosis is an angiogenic disease.

Claim 22 of the auxiliary requests 1 to 3, claim 23 of the auxiliary request 4 and claim 21 of the auxiliary request 5 were all considered to lack clarity within the meaning of Article 84 EPC.

The Opposition Division took the view that a lack of clarity arose from the wording of the use claim which was not a literal combination of claims 27 and 28 as granted.

IV. The appellant (patentee) lodged an appeal against the said decision.

V. A communication was sent to the parties on 15 March 2002. The appellant was invited to confirm that its sole request corresponded to the maintenance of the

patent as amended on the basis of the set of claims filed with the grounds of appeal on 21 December 2000. It was also invited to confirm that the use claims were abandoned. The parties were informed that if that were the case the appeal could be admissible. They were also informed that the Board envisaged a remittal of the case to the first instance for the examination of the subject-matter of the product claims. The parties were invited to inform the Board whether they would maintain their requests for oral proceedings since novelty and inventive step would not be subject of such oral proceedings.

VI. The appellant confirmed in its letter of 24 May 2002 that its sole request corresponded to the maintenance of the patent as amended on the basis of the set of claims filed with the grounds of appeal of 21 December 2000. It further confirmed that the use claims were no longer the subject of this appeal. It agreed that the case should be remitted to the Opposition Division and withdrew its request for Oral Proceedings before the Board under the circumstances depicted in the communication.

Claim 1 of the main request 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."

It contended that the amended claims did not offend Article 123(2) or Article 123(3) EPC. Moreover, the amended claim 1 was clear and did not offend Article 84

EPC. The CAM assay was not solely disclosed in the application as filed in a general manner (cf. paragraph bridging pages 9 and 10), specific exemplification of this assay being provided in Example 2. Furthermore, at the priority date of the contested patent the CAM assay was common general knowledge and was well-known to those skilled in the art. The introduction into claim 1 of the reference to the CAM assay is a restrictive amendment. The amended claim 1 was restricted to those compounds which exhibit an anti-angiogenic effect in the CAM assay.

VII. Respondent opponent V denied that the amended claims were allowable within the meaning of Article 123(2), Article 84 and Article 83 EPC. It contended that the feature that the active be "anti-angiogenic by the CAM assay" was not clear, that the said feature owed nothing to the invention and that the claim was not enabled across its scope. It further stated that the patent as granted asserted that several compounds, including colchicine and methotrexate, were anti-angiogenic factors by the CAM assay. In the statement of grounds of appeal the patentee admitted for the first time that both those compounds fail the CAM assay. If the patentee itself was so unclear about the scope of its claim, how could the claim be sufficiently clear for third parties to be able to understand the scope? The patentee had provided no evidence to show that a positive result in the CAM assay bears any relation to a beneficial effect on stents as claimed in the present application. The only data provided related entirely to taxol. The person skilled in the art must conduct further experiments to assess whether any particular compound, even amongst those specifically mentioned in the patent in suit,

fall within the scope of the claim. It was still unclear as to whether or not heparin is supposed to be within the definition "anti-angiogenic by the CAM assay".

Furthermore the result of the assay was highly dependent upon the dosage of active which is applied. There was no guidance in the specification regarding dosages. Still further, there was no indication that the dosage of drug for the CAM assay bears any relation to the dosage applied to the claimed stent. No guidance was provided and the claims had no reference to either dosage. If the CAM assay was to be carried out using a stent there was no suggestion as how this should be done.

Respondent opponent III stated that, as expressed during the opposition proceedings, the CAM assay was a well-known standard test. It was used to avoid assays on animals. Such a test belonged to the general knowledge and was a well known tool for the skilled person in the pharmacological field. The skilled person would know how to find an appropriate coating for the stent, using among other measures the CAM assay. This was a routine measure which lacks an inventive step.

VIII. The appellant requested that the decision under appeal be set aside and that the patent be maintained with the set of claims filed with the grounds of appeal of 21 December 2000.

Apart from opponent I, which made no requests during the appeal proceedings, the respondents all requested that the appeal be dismissed.

Respondents opponents IV and V also requested the remittal of the case to the first instance for a decision on the product claims.

Respondent opponent V further requested, in the event of remittal, an apportionment in its favour of the costs of the appeal and of any further proceedings before the Opposition Division.

IX. None of the parties maintained its previous request for oral proceedings to be held before the Board of Appeal.

Reason for the Decision

1. *Admissibility of the appeal*

The appellant has confirmed that it no longer pursues the use claims which served as the basis of the Opposition Division decision and that its sole request is the set of claims filed with the grounds of appeal which only contains product claims. The deletion of the use claims took place in response to the contested decision. The appellant's efforts are directed to the product claims which have not been examined by the Opposition Division and which did not form any basis for the decision under appeal. The product claims were however attacked by the opponents during the opposition proceedings and thus fall within the framework of the appeal proceedings. The appeal is admissible.

2. *Article 84*

The wording of claim 1 may be structured as follows:

a1 a **stent** (for expanding the lumen of a body passageway)
the stent comprising:
a2 a generally **tubular structure**
a3 **coated** with a composition

the coating composition is defined as comprising:
b1 an **anti-angiogenic** factor and
b2 a polymeric carrier,

the factor is defined as:
c1 being anti-angiogenic by the CAM assay.

The review article D39 (published July 1991), which relates to "Inhibitors of angiogenesis", confirms the existence of the CAM (chick chorioallantoic membrane) assay as a standard *in vivo* test before the priority date of the patent in suit (cf D39, page 630, right column, line 28 and page 631, left column, second paragraph). Additionally, the statement: "The angiogenesis inhibition was demonstrated in a **commonly used assay** (*emphasis added*) using chick chorioallantoic membrane" made in D47, cf column 7, lines 28-30, further confirms this.

The Board is satisfied that the CAM assay, as has been acknowledged by respondent opponent III during the appeal proceedings, belongs to the general knowledge of the skilled person in the pharmacological field and is a standard test to be used in order to avoid tests on animals.

It is clear from the wording of the claim that it is the "anti-angiogenic factor" used as component of the coating composition which is to be tested by the CAM

assay. A positive result by the CAM assay is necessary in order that a substance is considered to be an "anti-angiogenic factor" within the meaning of claim 1.

Compared with claim 1 as granted, claim 1 is restricted insofar as it no longer includes as components for the coating composition those substances which do not give positive results by the CAM assay. In other words, there may be substances that give positive results by other tests for anti-angiogenesis (for instance *in vitro* assays as those listed on page 631 of D39) but negative results by the CAM assay. Such substances are no longer encompassed by amended claim 1 as components for the coating composition. This analysis is confirmed by the statement: "A variety of methods may be readily utilized to determine the anti-angiogenic activity of a given factor, including for example, chick chorioallantoic membrane (CAM) assays" appearing on page 9, lines 34 to 36 of the description as filed.

It is a fact, however, that claim 1 remains silent about the dosage to be tested by the CAM assay. Therefore the choice of the anti-angiogenic factor to be used as component for the coating composition may be made among substances giving positive results by the CAM assay (i.e. tests results showing avascular zones) at a certain (not specified) dosage. Nevertheless, it has to be considered that there are limits, with respect to the dosage, set by the technique itself, e.g. a too low or a too high dosage may lead to negative results (i.e. no effect or death of egg respectively). The wording of the claim only requires a skilled person in the pharmacological field to establish by routine experiments whether a substance gives positive anti-angiogenesis results by the CAM

assay or not.

In conclusion, the fact that the dosage is not defined in the claim does not lead to a lack of clarity.

With regard to respondent opponent V's arguments that claim 1 is silent about the amounts of anti-angiogenic factor used for the coating composition (either in relative or in absolute terms with respect to the stent), the Board observes that this was also the case with claim 1 as granted. The absence of amounts in claim 1 means that it encompasses stents comprising a tubular structure coated with a composition in which the anti-angiogenic factor may be present in any conceivable amount suitable for the function stated in the claim and related to the **coating** of the stent with the further condition that the stent has to be suitable for expanding the lumen of a body passageway. Accordingly, the mention of the CAM assay for assessing the anti-angiogenic activity of one of the components of the coating composition restricts the nature of the substance to be used but does not restrict its amount in the said composition. The fact that the dosage remains undefined in the claim means that the claim encompasses all technically meaningful possibilities. Hence, claim 1 does not lack clarity with respect to the dosage of the anti-angiogenic factor to be used.

As regards the fact that the test results depend on the dosage, this applies to any activity tests in the pharmacological field. However, the consequence is not that claim 1 is obscure, but that claim 1 is broadly defined. Furthermore, the suggestion by respondent opponent V of the possibility of performing a CAM assay when the factor is on the stent appears technically

implausible given the nature and form of the assays.

With respect to respondent opponent V's argument relating to the deletion of claim 3 as granted, in which methotrexate was specifically mentioned as an anti-angiogenic factor, the following has to be said. There is no contradiction between the fact that claim 1 has been restricted in respect to the nature of the anti-angiogenic factor and the deletion of claim 3. It has been shown by the appellant (cf test results filed during the appeal procedure) that methotrexate does not give positive results in the CAM assay. Hence, methotrexate is clearly not encompassed by amended claim 1. Whether methotrexate may or may not show anti-angiogenic properties by other tests (for instance *in vitro* tests) has not been proven by the respondent and is irrelevant for the assessment of amended claim 1. Contrary to respondent opponent V's assertion, it cannot be seen where in the description of the patent in suit colchicine or methotrexate were disclosed as anti-angiogenic factors by the CAM assay. But even if methotrexate were listed as an option for anti-angiogenic factor by the CAM assay, the skilled person would immediately know, after performing routine tests, whether or not that piece of information supposedly appearing in the description was correct. This is no reason for challenging the clarity of the amended claim.

As regards the objection that it is unclear whether heparin is encompassed by the definition "anti-angiogenic factor by the CAM assay" or not, the following has to be said. It has to be tested by the CAM assay. The tests provided by the appellant with its grounds of appeal do not show positive results for

heparin by the CAM assay. Respondent opponent V has not provided any technical proof challenging any of the test results.

Claim 1 as amended requires routine tests to assess whether a certain substance falls within the definition given in the claim or not. However, this is usually the case for functional definitions, which are commonly used in claims in the medical field. Moreover, the restriction of the subject-matter claimed is an allowable procedural step which might require subsequent adaptation of the description. The fact that the description has not yet been adapted to the amended claims cannot be used as ground for lack of clarity of the claimed subject-matter.

Finally, many of the arguments put forward by respondent opponent V under the headnote "clarity and sufficiency" (cf. in particular the paragraphs 5.4, 5.6, 5.7, 5.8 of the letter of 14 May 2001) relate to an assessment of the requirements of Articles 83, 54 and/or 56 EPC. These arguments may be advanced before the first instance, as and when appropriate, when the product claims are considered.

In view of the above the Board has come to the conclusion that amended claim 1 meets the requirements of Article 84 EPC.

3. *Article 123 EPC*

With respect to the requirements of Article 123(2) EPC, the basis for the amendment specificying the CAM assay as the method for assessing the anti-angiogenic activity appears in the original disclosure on pages 9

and 10 of the description as filed.

Amended claim 1 concerns a restriction of the scope of claim 1 as granted in respect to the anti-angiogenic factor to be used as a component of the coating compositions. Furthermore claims 2 and 3 as granted have been deleted, as well as the use claims. Claims 4 to 15 as granted were dependent on claim 1 as granted. Therefore the deletion of claims 2 and 3 and the renumbering of the claims does not cause an extension of the subject-matter claimed in claims 4 to 15 with respect to the granted version. Thus the requirements of Article 123(3) EPC are met.

4. *Article 111(1) EPC.*

Article 100(b) was stated and substantiated as a ground of opposition. However, no decision was taken by the first instance as to sufficiency of disclosure. Furthermore, the product claims were not examined by the Opposition Division during the opposition proceedings and did not serve as any basis for the decision to revoke the patent. Therefore a remittal to the first instance will ensure two instances for the examination of the essential issues of the product claims (Articles 83, 54 and 56 EPC).

Furthermore respondents, opponents IV and V have requested remittal of the case to the Opposition Division for a first instance decision on the product claims; and the appellant has agreed to such remittal in response to the Board's communication.

In these circumstances the Board makes use of its power under Article 111(1) EPC to remit the case to the

Opposition Division for further prosecution.

5. *Apportionment of costs*

Respondent opponent V's request for an apportionment of costs in the event of such a remittal is based on the allegation that costs (by implication, unnecessary additional costs) have been created by the appellant having filed substantially different requests on appeal and that this is an abuse of procedure. That additional costs are occasioned by a remittal is clear but it would be difficult for the Board to decide now whether the appellant's behaviour was an abuse of procedure or a legitimate reaction to the decision under appeal, and as if not more difficult to decide now whether or not such behaviour has caused respondent opponent V to incur unnecessary costs or not. In all probability, respondent opponent V's costs of this appeal will have been related not only to the limited issues decided in this appeal but also to issues which remain to be decided in the further first instance proceedings - to decide now whether or not those latter costs were incurred unnecessarily would be speculative.

Further, respondent opponent V seeks not just its costs of this appeal but those of the further first instance proceedings. While it may be appropriate for a Board to make such a future costs order when a remittal results from an entirely fresh case on appeal (see for example T 0715/95, unreported in OJ EPO, in which an appellant relied only on new evidence introduced on appeal and the resulting remittal effectively meant the opposition proceedings had to be recommenced), it is far less appropriate when, as here, both the extent to which a remitted case may have to be re-litigated and

the extent to which that could have been avoided are unclear. Those matters will be far easier to decide after rather than before the further first instance proceedings.

A further consideration is that the other respondents have not made requests for apportionment of costs but might wish to do so in due course and that the appellant has not answered respondent opponent V's allegations or request. To prolong this appeal by argument over its costs would in itself lead all parties to incur additional but avoidable costs.

Accordingly the Board, while expressing no opinion as to the correctness or otherwise of the appellant's behaviour or respondent opponent V's request, considers the appropriate time for a decision on apportionment of costs to be the end of the further first instance proceedings. This will allow all parties to make such costs requests as they think fit and permit the Opposition Division to consider, when all the issues have been decided, whether there should be an apportionment of costs and, if so, in respect of which part or parts of the proceedings. The Board therefore refuses respondent opponent V's request for apportionment of costs so that all issues of costs can be dealt with at the most appropriate time (with the possibility of subsequent appeal). This is consistent with the Board's earlier decision T 0048/00 (unreported in OJ EPO) in which, in different circumstances but for

similar reasons, a request for apportionment of the appeal costs of a remitted case was deferred to the further first instance proceedings.

Order

For these reasons it is decided:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance for further prosecution.

3. Respondent opponent V's request for an apportionment of costs is refused.

The Registrar: The Chairman:

A. Townend U. Oswald