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D E C I S I O N
of 12 April 2002

Case Number: T 0146/98 - 3.3.2

Application Number: 89906659.1

Publication Number: 0420877

IPC: A61K 31/79

Language of the proceedings: EN

Title of invention:
A method and composition for preventing surgical adhesions

Patentee:
UNIVERSITY OF FLORIDA

Opponent:
Johnson & Johnson
FIDIA, S.p.A.

Headword:
Surgical Adhesions/UNIVERSITY OF FLORIDA

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
"Main and auxiliary requests - added matter: yes - amendment introducing a technical relationship between molecular weight and concentration which was not originally disclosed"

Decision cited:
T 0201/83

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0146/98 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 12 April 2002

Appellant: (Proprietor of the patent)
UNIVERSITY OF FLORIDA
223 Grinter Hall
Gainesville
Florida 32611-2037 (US)

Representative:
Hedley, Nicholas James Matthew
Kilburn & Strode
20 Red Lion Street
London WC1R 4PJ (GB)

Respondents: (Opponent 01)
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick
New Jersey 08903 (US)

Representative:
Mercer, Christopher Paul
Carpmaels & Ransford
43, Bloomsbury Square
London WC1A 2RA (GB)

(Opponent 02)
FIDIA, S.p.A.
Via Ponte della Fabbrica 3-A
I-35031 Abano Terme (Padova) (IT)

Representative:
Desaix, Anne
Ernest Gutmann - Yves Plasseraud S.A.
3, rue Chauveau-Lagarde
F-75008 Paris (FR)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 12 December 1997 revoking European patent No. 0 420 877 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: P. A. M. Lançon

Members: J. Riolo
S. U. Hoffmann

Summary of Facts and Submissions

I. European patent No. 0 420 877 based on application No. 89 906 659.1 was granted on the basis of 6 claims.

Independent claims 1 and 5 as granted read as follows:

"1. Use of a hydrophilic, water soluble, biocompatible, pharmaceutically acceptable polyelectrolyte polysaccharide having a molecular weight of at least 500,000 (which polysaccharide is not hyaluronic acid having a molecular weight greater than 1,500,000) or a pharmaceutically acceptable salt of the said polysaccharide or a mixture thereof in the preparation of a physiologically acceptable aqueous solution of said polysaccharide, salt or mixture thereof in a concentration of from 0.01% to 15% by weight (the said molecular weight and the said concentration being such that the solution is capable of providing wet coatings on tissue surfaces) for preventing post-operative surgical adhesions of tissue involved in surgery by providing surfaces of the said tissue with a wet coating of the said solution prior to manipulation of the tissue during surgery.

5. Use of a hydrophilic, water soluble, biocompatible pharmaceutically acceptable hyaluronic acid or a pharmaceutically acceptable salt thereof (or a mixture thereof) having a molecular weight of at least 1,500,000 in the preparation of a physiologically acceptable aqueous solution of said hyaluronic acid or salt thereof (or mixtures thereof) in a concentration of from 0.01% to 1% by weight (the said molecular weight and the said concentration being such that the solution is capable of providing wet coatings on tissue

surfaces) for preventing post-operative surgical adhesions of tissue involved in surgery by providing surfaces of said tissue with a wet coating of the said solution prior to manipulation of the tissue during surgery."

II. Notices of opposition were filed against the granted patent by the respondents (opponent O1 and opponent O2).

The patent was opposed under Article 100(a) and (b) EPC.

III. The Opposition Division took the view that the set of claims of the patent as granted did not meet the requirements of Articles 52(1) and 56 EPC and revoked the patent under Article 102(1) EPC by its decision pronounced on 21 October 1997.

The Opposition Division examined, of its own motion, the allowability of the set of claims as granted with respect to Article 123(2) EPC. In that respect, it concluded that the disclaimers introduced in claims 1 and 5 during the examination procedure should not have been allowed as they did not fulfil the requirements of Article 123(2) EPC. It however decided not to object to them as they did not introduce relevant technical features into these claims.

As for the objections pursuant to Articles 83 and 52(4) and to novelty, the Opposition Division considered that they were ill-founded.

The Opposition Division concluded however that document (1) *(Arch. Surg.,* 115, p. 776-780), representing the

closest state of the art and showing that application of a high molecular weight polymer coating before manipulation was advantageous over post-coating, rendered obvious the claimed subject-matter which involved the use of a solution of a high molecular weight polysaccharide in the light of document (3) (US-A-4 141 978).

The problem to be solved over document (1) was seen in the provision of alternative high molecular weight polymers.

As document (3) disclosed high molecular weight polysaccharides (ie hyaluronic acid) for the same type of application as in the patent in suit, it was considered obvious to use such polymers to solve the above problem.

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

VII. The Board gave its preliminary view with respect to Article 123(2) in two communications dated 4 October 2000 and 21 June 2001.

VIII. In response to these communications, the appellant filed a set of 12 claims with three independent claims as auxiliary request 2A with its letter of 12 March 2002.

Independent claim 4 of this set of claims read as follows:

"4. Use of a hydrophilic, water soluble, biocompatible, pharmaceutically acceptable hyaluronic acid or a

pharmaceutically acceptable salt (or a mixture thereof) having a molecular weight of at least 500,000 and not greater than 1,500,000 in the preparation of a physiologically acceptable aqueous solution of said hyaluronic acid or salt thereof (or mixture thereof) in a concentration of from 0.01% to 15% by weight (the said molecular weight and the said concentration being such that the solution is capable of providing wet coatings on tissue surfaces) for preventing post-operative surgical adhesions of tissue involved in surgery by providing surfaces of the said tissue with a wet coating of the said solution prior to manipulation of the tissue during surgery."

IX. Oral proceedings were held before the Board on 12 April 2002.

During the oral proceedings the appellant submitted an auxiliary request replacing auxiliary request 2A which corresponded to this latter request wherein the feature "from 0.01% to 1%" was replaced by "from 0.01% to less than 1%" in claim 3 at line 5.

X. As regards Article 123(2), the appellant submitted that the amendments introduced in the claims were supported by the original disclosure in the description (page 10, line 22, to page 11, line 14) and also by Example 3. It moreover maintained that it should be, in any case, allowable to disclaim protection for a part of the range originally claimed.

XI. The arguments of the respondents submitted both in the written procedure and at the oral proceedings can be summarised as follows:

In their view, claim 1 and claim 5 as granted and, among others, claim 4 of the request submitted during oral proceedings contravened Article 123(2) because no verbatim support for the amendments could be found in the application as filed. They moreover maintained that the molecular weight disclosed in example 3 of the description could not be extended to the whole concentration range recited in claim 1 of the main request and claim 4 of the auxiliary request.

XII. The appellant requested that the decision under appeal be set aside and that the patent be maintained as granted (main request) or with the request submitted during the oral proceedings (auxiliary request) which corresponds to the request filed on 12 March 2002 wherein the feature "from 0.01% to 1%" is replaced by "from 0.01% to less than 1%" in claim 3, line 5.

The respondents requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. *Main request*

2.1 Article 123(2)

2.1.1 In essence, the subject-matter of claim 1 differs from the subject-matter as originally filed in that the polymeric material is restricted to polyelectrolyte polysaccharides and in that, in the case of polyelectrolyte polysaccharide hyaluronic acid, a molecular weight range of at least 500 000 to 1 500 000

is now associated with a concentration range of 0.01% to 15% by weight.

It thus appears that a technical relationship now exists between a specific molecular weight of hyaluronic acid, ie 1 500 000, and a concentration range. Thus, below this specific molecular weight of 1 500 000, the concentration of hyaluronic acid varies between 0.01% and 15% by weight, whereas above this specific molecular weight hyaluronic acid is disclaimed.

As there is no verbatim basis for this technical relationship, it must be decided whether the skilled person could however derive it directly and unambiguously from the whole teaching of the application as originally filed.

The following passages in the application as originally filed mention hyaluronic acid and a molecular weight of 1 500 000 and are therefore relevant for assessing the question of added matter:

- page 10, line 22, to page 11, line 14:

"...Although naturally occurring HA with molecular weight greater than 1,000,000 has been used clinically as a gel in ophthalmic surgery to maintain the anterior chamber, such gels require HA concentrations of 1.0% or more and because of their extremely high viscosity are not readily applied as tissue-protective irrigating solutions according to the method of this invention... Unexpectedly, we have discovered that dilute HA solutions of HA with molecular weight >500,000 are highly effective at concentrations of 0.01 to 0.6%, by

weight, when used for surgical adhesion prevention as taught herein... As indicated in the following examples, even a 0.01% solution of about 1,500,000 molecular weight HA effectively prevents all severe intra-abdominal adhesions in a rat adhesions model that normally produces more than 70% adhesions."

- Example 3

"This example illustrates the significant reduction in adhesions achieved by the use of the aqueous high molecular weight hyaluronic acid (HA) solutions with the surgical method as taught herein. The abdominal surgery rat procedure of Example 1 was used with aqueous test solutions prepared at various concentrations (wt. %) with sodium hyaluronate (Genzyme, mol. wt. ca. 1,500,000). The following summarizes the scoring of adhesions for the HA solutions:

Test Solution/	# of Test Animals/	Significant % Adhesions (scored 2 or greater)
0.05% Ha	10	10%
0.1% Ha	10	0%
0.3% HA	18	17%
0.6% HA	19	0%
0.8% HA	10	10%
Ringer's lactate (control)	15	73%

Using tissue coating prior to surgical manipulation, the HA solutions effect a major reduction in surgical adhesions, even at extremely low concentrations (no significant adhesions with 0.1% HA) as compared with 73% of significant adhesions for the control group of Example 1 in which a conventional surgical irrigating

solution was employed in the same procedure."

From these passages, it is apparent that a solution containing hyaluronic acid having a molecular weight of 1 500 000 in a weight concentration of 0.01%, 0.05%, 0.1%, 0.3%, 0,6%, 0.8% is effective.

It can also be inferred from the first sentence of the description referred to above that hyaluronic acid having a molecular weight no greater than 1 500 000 in a weight concentration of 0.01% to 0.8% is also effective as the skilled person knows than the viscosity will decrease when the molecular weight decreases (ie "Although naturally occurring HA with molecular weight greater than 1,000,000 has been used clinically as a gel in ophthalmic surgery to maintain the anterior chamber, such gels require HA concentrations of 1.0% or more and because of their extremely high viscosity are not readily applied as tissue-protective irrigating solutions according to the method of this invention").

It cannot however be inferred that the viscosity will also be suitable when the weight concentration varies between greater than 0.8% and 15%. On the contrary, as a molecular weight of hyaluronic acid greater than 1 000 000 in relation to a concentration of 1.0% is disclosed in the application as filed as having an extremely high viscosity and as being not readily applicable as tissue-protective irrigation, it must be concluded that the skilled person could not infer this technical relationship for the all weight concentration range directly and unambiguously from the whole teaching of the application as originally filed.

In view of the above considerations, the Board sees no basis for the introduction of the technical relationship between the specific molecular weight range of hyaluronic acid, ie between greater than 500 000 and not greater than 1 500 000, and the concentration range 0.01% to 15% in independent claim 1, which contravenes Article 123(2) EPC

2.1.2 Contrary to the appellant's opinion, it is not accepted that the value 1 500 000 given in Example 3 of the application as originally filed constitutes a proper base for limiting the claimed range. As correctly mentioned by the applicant, it is established European practice that the top or bottom limits in a range in a claim can be amended to a value given in an example **so long as the skilled person would understand that the value from the example is applicable to the whole invention as claimed and not just the particular example** (T 201/83, OJ EPO 1984, 481, points 6 and 9). This is not however the case in the present particular circumstances since, as highlighted in Example 3 and in the description on page 10, line 22, to page 11, line 14, and as indicated by the applicant himself (applicant's letter dated 13 February 2001, paragraph 3.4), a technical relationship does exist between the molecular weight of hyaluronic acid and its concentration in order to avoid excessive viscosity with respect to its intended use.

3. *Auxiliary request*

Claim 4 of this request corresponds in fact to claim 1 of the main request which has been merely restricted to hyaluronic acid. Accordingly, the above reasoning holds

good for this set of claims as well.

4. As regards the appellant's request made in writing "that the question of whether an applicant, voluntarily giving up protection for part of the original protection..., contravenes Article 123(2) EPC should be referred to the Enlarged Board of Appeal", should the objection under Article 123(2) EPC be upheld, the Board notes that this request was not maintained during the oral proceedings (appellant's letter of 31 October 2001, page 2, paragraph 7).

In this connection, the Board wishes however to point out that it does not deny that a voluntary limitation of the scope of the protection does not necessarily contravene Article 123(2).

Nevertheless, as would appear from the above discussion under point 2.1, the present amendments do not amount to a mere limitation of the scope of the protection, but rather to a new definition of the invention for which no basis could be found in the application as originally filed, so that the question mentioned above is not relevant to the present case.

Order

For these reasons it is decided that:

The appeal is dismissed-

The Registrar: The Chairman:

A. Townend P. A. M. Lançon