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**Datasheet for the decision
of 21 February 2008**

Case Number: T 0841/04 - 3.3.04

Application Number: 92913177.9

Publication Number: 0590015

IPC: A61K 38/36

Language of the proceedings: EN

Title of invention:

Tissue treatment composition comprising fibrin or fibrinogen
and biodegradable and biocompatible polymer

Patentee:

Wadström, Jonas

Opponent:

Baxter International Inc.

Headword:

Tissue treatment composition/WADSTRÖM

Relevant legal provisions:

EPC Art. 54, 56, 123(2)

Keyword:

"Main request (claims as granted): added subject-matter (no);
novelty and inventive step (yes)"

Decisions cited:

-

Catchword:

-



Case Number: T 0841/04 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 21 February 2008

Appellant:
(Patent Proprietor)

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Decision under appeal:

Interlocutory decision of the Opposition
Division of the European Patent Office posted
3 May 2004 concerning maintenance of European
patent No. 0590015 in amended form.

Composition of the Board:

Chairman: R. Moufang
Members: G. Alt
R. Gramaglia

Summary of Facts and Submissions

- I. This is an appeal by the patent proprietor (appellant) against the opposition division's decision that European patent No. 0 590 015, entitled "Tissue treatment composition comprising fibrin or fibrinogen and biodegradable and biocompatible polymer" could be maintained in amended form pursuant to Article 102(3) EPC 1973.
- II. The patent had been granted with twenty-three claims, nine of them relating to a tissue treatment composition, nine to the use of this composition and five to a preparation consisting of two components which when mixed will form the tissue treatment composition.

Claim 1 as granted read:

"1. A tissue treatment composition comprising
(i) fibrin, fibrinogen or a combination thereof;
(ii) Factor XIII;
(iii) thrombin; and
(iv) a viscosity enhancing polysaccharide or proteoglycan, which do not negatively interfere with the clotting process and which is [sic] present in sufficient amount so that a viscous aqueous solution can be formed."

- III. The opposition was based on Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC) and on Article 100(c) on the ground of added subject-matter (Article 123(2) EPC).

IV. The opposition division decided that the claims of the patent as granted (main request) fulfilled the requirements of Article 123(2) EPC. It reasoned that the term "a viscosity enhancing polysaccharide or proteoglycan" in claim 1 had a basis in the description as filed on page 3, lines 22 to 28.

However, the opposition division held that the subject-matter of claim 1 as granted was not novel over the disclosure in document D1. In particular, the opposition division held that the expression within the functional feature of the claim (point iv) "can be formed" was not limiting and did not imply that a viscous aqueous solution actually was formed. Moreover, there was an indication in document D1 that the purpose of mixing the components was to form a gel which was per definitionem a viscous solution.

Auxiliary request I was found not to fulfil the requirement of Article 83 EPC. Auxiliary request II was found to comply with the requirements of the EPC.

V. With the statement of the grounds for appeal the appellant filed retyped claims as granted (entitled "Main Request (claims as granted)") as a main request and four auxiliary requests. It requested that the decision of the opposition division be set aside and that the patent be maintained as granted or on the basis of one of the four auxiliary requests. Oral proceedings were requested as an auxiliary measure. This latter request was withdrawn by letter dated 1 February 2008.

VI. The respondent informed the board that it would not be filing a response to the appeal. Oral proceedings were also requested. This request was withdrawn by letter dated 12 February 2008.

VII. Oral proceedings took place on 21 February 2008 in the absence of both parties. At the end of the proceedings the board announced its decision.

VIII. The following documents are cited in the present decision:

D1: US 4,837,379

D2: EP-A-0 305 243

D3: EP-A-0 253 198

D4: Int. J. Tiss. Reac., vol. X, no. 6, 1988, pages 355-365, Weigel, P.H. et al.

D5: Ciba Foundation Symposium, 143; Editors: David Evered and Julie Whelan, 1989, pages 248-264, Weigel, P.H. et al.

D6: Biochemistry, vol. 26, 1987, pages 6052-6057, LeBoeuf, R.D. et al.

D8: EP-A-0 373 044

D9: J. Surgical Research, vol. 40, 1986, pages 510-513, Barton, B. et al.

D10: EP-A-0 312 208

D14: The Art of Tisseeling - History, background, application techniques and indications of fibrin sealing in modern surgery; 1987, Immuno AG

- IX. The appellant's arguments submitted in writing before the opposition division and the board, as far as they are relevant for the present decision, may be summarised as follows:

Main request

Added subject-matter

The opposition division correctly ruled that the claims as granted comply with the requirements of Article 123(2) EPC. It was derivable from the application as filed that biodegradability and biocompatibility was a mandatory property of all the polymers used for enhancing the viscosity of the claimed tissue treatment composition, i.e. also of the polysaccharides and proteoglycans mentioned in claim 1 and that therefore, even if these properties were not explicitly stated in the claims as granted, their subject-matter did not extend beyond the content of the application as filed.

Novelty

Tissue equivalents comprising the four components mentioned in points (i) to (iv) of claim 1 were not clearly and unambiguously disclosed in document D1. Moreover, the tissue equivalents disclosed in the document were solid lattices and not viscous aqueous

solutions like the claimed tissue treatment compositions. Therefore, the disclosure of document D1 did not anticipate the claimed subject-matter.

Inventive step

Either of the commercial fibrin sealants (as exemplified by documents D2, D3, D8 and/or D9 and as mentioned in paragraph [0009] of the patent) was to be considered as the closest prior art.

Neither of documents D4 to D6 or D10 gave a pointer to the claimed solution. Document D10 dealt with the problem of controlled delivery of growth factors during wound healing. Documents D4 to D6 related to the role of endogenous hyaluronic acid and its interaction with fibrin during the natural wound healing and inflammation process.

- X. The respondent's arguments submitted during the opposition proceedings and as far as they are relevant for the present decision may be summarised as follows:

Main request

Added subject-matter

It was stated in the application as filed that the tissue treatment composition comprised biodegradable and biocompatible polymers. Since this limitation was not included expressis verbis in claim 1 as granted, the claim encompassed compositions which did not have these properties. Therefore, the claim related to

subject-matter not comprised in the content of the application as filed.

Novelty

Document D1 disclosed tissue equivalents comprising inter alia fibrin, thrombin, factor XIII and hyaluronic acid. Since the composition according to claim 1 also comprised these compounds and since, in the light of claim 9 relating to a film or a sheet, claim 1 could not be considered as being limited to viscous aqueous solutions, the claimed subject-matter was not novel over the disclosure in document D1. Moreover, document D1 also disclosed a gel with the same constituents, a gel being per definitionem a viscous aqueous solution.

Inventive step

The handling problems due to the water-like consistency of the known fibrin sealants being known, it was obvious for the skilled person to include a viscosity enhancing compound such as hyaluronic acid as disclosed in document D10. Moreover, it was known from documents D4 to D6 that hyaluronic acid had advantageous effects during the natural wound healing process. That was a further reason to include it in a tissue treatment composition.

Reasons for the Decision

1. Although both parties had withdrawn their requests for oral proceedings, the board considered it expedient to

hold them as scheduled pursuant to Article 116(1) EPC for reasons of procedural efficiency.

2. According to Article 15(3) of the Rules of Procedure of the Boards of Appeal (RPBA), a board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned, who may then be treated as relying only on its written case. In the present case the board could therefore take a decision at the oral proceedings, notwithstanding the absence of both of the duly summoned parties.

Main request

3. The board has noted that the retyped main request, submitted with the statement of the grounds for appeal, and the granted claims as published differ in that claim 5 of the retyped version refers to "claims 1 to 3" instead of to "claims 1 to 4" as does claim 5 of the published version. In addition, claim 9 of the published version has a reference to "claim 1 or 2" whereas claim 9 of the retyped version refers to claim 1 only.

- 3.1 Throughout the appeal proceedings the appellant has requested, as a main request, consideration of the claims as granted (submission dated 2 July 2004 (notice of appeal); submission dated 13 September 2004 (grounds of appeal) referring in point I.3 to the "Main Request (Annex I)" which is the retyped request and which is entitled "Main Request (claims as granted)"). In point II.1.1 of the grounds of appeal, the appellant furthermore stated: "The Main Request in Annex 1 is

identical to the Main Request considered by the OD and relates to the claims as granted.". Also in its submissions dealing with the patentability requirements of the claims of the main request, the appellant refers to the claims as granted (for example page 5, point II.2.1.1; title of point II.2.2; page 13, point II.2.5.5). Under these circumstances the board is convinced that the above-mentioned differences are typographical errors rather than intentional amendments and has consequently considered the granted claims of the published version in the present decision.

Added matter

4. In the decision under appeal the opposition division held that the main request before it, which corresponds to the main request considered here, i.e. the claims as granted, complies with the requirements of Article 123(2) EPC. The board agrees. When interpreting the claims in the light of the description (see paragraph [0018]: "A preferred group of said biodegradable and biocompatible polymers, hereinafter frequently referred to as viscosity enhancing polymers, consists of high molecular polyglycans or polysaccharides. Exemplary of such polysaccharides for the purposes of the invention are ... proteoglycans, ...") the skilled person would understand the expression "a viscosity enhancing polysaccharide or proteoglycan, which do not negatively interfere the clotting process" as referring to a subgroup of biodegradable and biocompatible polymers.

Novelty

5. Claim 1 defines a tissue treatment composition which comprises inter alia "a viscosity enhancing polysaccharide or proteoglycan [...] which is present in sufficient amount so that a viscous aqueous solution can be formed" (point (iv) of claim 1; see section II above).
- 5.1 The question arises whether in the context of claim 1 the feature "so that a viscous aqueous solution can be formed" defines solely the amount of viscosity enhancing compound present in the composition, or whether it also characterises the physical state of the tissue treatment composition per se. A further question is whether or not, due to the wording "**can** be formed" (emphasis by the board) the feature denotes merely a potential property of the tissue treatment composition, i.e. that it can or cannot be in the form of a viscous aqueous solution.
- 5.2 For the interpretation of a patent claim, account is taken of the perspective of the skilled person reading the claim in the context of the patent in its entirety. Therefore, the skilled person would not give an interpretation to a claim which contradicted the overall technical teaching of the patent.
- 5.3 The patent relates to fibrin-based tissue adhesives or tissue sealants which are used as haemostatics, tissue glues and wound healing compositions (paragraphs [0001] and [0007]). Generally, these adhesives are based on two components, fibrinogen and thrombin. When both are mixed for use, fibrinogen is transformed to fibrin

through the action of thrombin. The fibrin monomers spontaneously polymerise to form a three-dimensional network (paragraph [0003]). The rate of polymerisation is dependent on the thrombin concentration (paragraph [0009]). The fibrin-based adhesives are commercially available e.g. as a two-part kit containing the components in separate containers, for example in two syringes (paragraphs [0009] and [0010]).

5.4 In particular, the patent relates to improving the handling properties of such adhesives which have a water-like consistence shortly after mixing, i.e. in the first moments of application, as a result of the fact that polymerisation is a continuous process and, depending on the thrombin concentration, may take from a few seconds up to a couple of minutes (paragraphs [0009] and [0010]). A too liquid state however causes problems, for example after application on vertical areas, because the substance tends to run off so that the clotting reaction cannot take place at the desired site (paragraph [0010]). Hence, according to the invention disclosed in the disputed patent, a viscosity-enhancing compound is included in the tissue treatment composition in order to keep it in place.

5.5 Thus, in the board's view, the skilled person would derive from the overall teaching of the patent as summarised above that the aqueous and viscous nature is an essential element of the ready-to-use form of the tissue treatment compositions according the patent.

Therefore, in applying the principle set out in point 5.2 above, the board comes to the conclusion, that, in the context of claim 1, the feature "so that a

viscous aqueous solution can be formed" does not only define the amount of the viscosity-enhancing agent, but that it also qualifies the tissue treatment composition per se. Moreover, interpreting this expression to mean that a viscous aqueous solution may not be formed would contradict the overall teaching of the patent and is therefore excluded. Consequently, the board interprets claim 1 as relating to a tissue treatment composition when it is a viscous and aqueous solution. Such a condition is present after the components have been brought into a state which allows coagulation to start and before the ongoing coagulation has changed the viscosity to an extent that the composition can no longer be considered as a viscous aqueous solution. Thus, the claim can neither be construed to relate to a composition in which coagulation has not yet started, nor to a composition where coagulation is completed.

5.6 This interpretation of claim 1 is not in contradiction with the meaning of claim 9 stating that the composition is "in the form of a film or sheet" because, in the board's view, this expression relates to the form in which the viscous aqueous solution is applied to the parts to be treated. It does not indicate, for example, that the composition is in the form of a prefabricated film or sheet.

6. Document D1 was cited against the novelty of the subject-matter of claim 1. It is a patent application disclosing so-called tissue equivalents. Moreover, a gel-like substance is disclosed which is generated as an intermediate product during the production of the tissue equivalents.

6.1 The tissue equivalents are used as substitutes for natural skin or blood vessels (columns 1 to 3 of document D1). They are essentially made from one or more layers of a hydrated collagen lattice contracted by a contractile agent such as fibroblast cells and fibrin (column 3). There may be other constituents such as hyaluronic acid and factor XIII (column 4).

Hyaluronic acid is the preferred viscosity enhancing agent according to the patent in suit (paragraph [0019]). Thus, in the board's view, document D1 indeed discloses all features mentioned in or falling under the definition of points (i) to (iv) of claim 1.

6.2 Nevertheless, the tissue equivalents disclosed in document D1 do not take away the novelty of the claimed product. It is apparent from the teaching of document D1 that the tissue equivalents disclosed therein, in their ready-to-use state, cannot be considered as aqueous viscous solutions, unlike the fibrin adhesives according to claim 1 of the main request (see point 5.5 above). This conclusion is supported by

- the composition of the product itself (see point 6.1 above) of which the main constituent is a collagen lattice;
- the disclosure, in document D1, of the underlying problem, which is to strengthen the tissue equivalents in order for them to be able to better withstand mechanical stresses, for example inter-vascular pressures (column 3, first full paragraph);
- the disclosure in Example 2 in column 8 where it is stated that each of the produced tissue

equivalents "was grabbed with a pair of forceps but they could not be pulled apart".

- the disclosure in Example 4 that a blood vessel substitute made according to the invention was "cut with a surgical scissors" (column 9, line 55).

Thus, since the physical nature of the tissue treatment composition is a technical feature of claim 1, i.e. a viscous aqueous solution (see point 5.5 above), the tissue equivalents according to document D1 and the claimed tissue treatment composition differ.

- 6.3 The gel which is formed as an intermediate product during the production process according to document D1 (see point 6 above) is generated by mixing collagen, fibrinogen and an agent which causes the formation of fibrin from fibrinogen, for example thrombin and at least one contractile agent, for example fibroblasts (column 4; example 1). However, the point in time at which during the production process factor XIII or hyaluronic acid are added, is derivable neither from the general description of the production process in document D1 (for example column 4) nor from the specific examples. Therefore, the board concludes that a gel having all the features recited in points (i) to (iv) of claim 1 is not clearly and unambiguously disclosed in document D1. Moreover, it is disclosed in document D1 that the gel is maintained under conditions which permit contraction of the gel to form the tissue equivalent (column 4, lines 31 to 33 and lines 47 to 49). Therefore, the board concludes that the gel-like substance does not serve the purpose indicated in claim 1, i.e. it is not a "tissue treatment composition". Consequently, the gel disclosed in

document D1 also is not detrimental to the novelty of the subject-matter of claim 1.

- 6.4 Thus, the subject-matter of claim 1 and its dependent claims 2 to 9 as well as of claims 15 to 23, relating to the use of said composition, is novel over the disclosure in document D1. The same is true for independent claims 10 and claims 11 to 14 dependent thereon because document D1 also does not disclose a preparation consisting of two components which when mixed will form the composition of claims 1 to 9.

The requirements of Article 54 EPC are fulfilled.

Inventive step

7. Either document D2 (as suggested by the respondent) or each of the known tissue adhesives as recited in paragraph [0009] of the patent in suit (as suggested by the appellant) may, in the board's view, be considered as the closest prior art, because they all relate to fibrin-based tissue treatment compositions which comprise fibrinogen/fibrin, factor XIII and thrombin. According to paragraph [0010] of the patent, such compositions are known to be difficult to handle due to their water-like state at the moment of application (see also the explanation in points 5.3 and 5.4 above).

- 7.1 Moreover, with regard to the above mentioned compositions the skilled person also knew at the priority date that the solidification time of these tissue adhesives was dependent on the thrombin concentration and therefore that running off from the desired site could be avoided by adapting said

concentration (see for example document D14, point 3.4). However, the skilled person was also aware of the problems connected to this approach, namely that the thrombin concentration could not be changed ad libitum because the setting rate of the adhesive had to be adapted to the desired application. It is for example disclosed in point 3.4 of document D14 that a high thrombin concentration and thus a fast solidification is advantageous to achieve haemostasis, while a lower thrombin concentration and thus a longer setting time is suitable for sealing tissues.

7.2 Hence, at the priority date of the patent the skilled person was confronted with the problem of providing alternative means for improving the handling problems of fibrin-based tissue adhesives occurring due to their too liquid state at the moment of application.

7.3 The respondent argued that the disclosure in documents D4 to D6 and D10 made the claimed solution, i.e. the inclusion of a viscosity-enhancing compound such as hyaluronic acid in a fibrin-based tissue adhesive, obvious.

7.4 The disclosure content of a document is determined from the perspective of the skilled person reading that document as a whole and without knowledge of the invention.

7.5 Thus, the board considers documents D4 to D6 and D10 to have the following disclosure content:

Documents D4 to D6 are scientific publications relating to the activity of endogenous hyaluronic acid and

fibrin in the early stages of the natural inflammatory response and of wound healing.

Document D10 is a patent application and deals with the problem of providing growth factors in a continuous way for promoting wound healing. Viscosity-adaptable carrier substances such as hyaluronic acid are mixed with growth factors to provide their sustained release.

7.6 The board considers therefore, in agreement with the opposition division in the decision under appeal, that upon proper interpretation none of documents D4 to D6 or D10 can be considered as proposing the inclusion of a viscosity-enhancing compound in fibrin sealants in order to avoid their running off in the first moments of application and thus the claimed solution.

7.7 The board concludes that the subject-matter of claim 1 and of the remaining claims, which are either dependent on claim 1 or refer to it, involve an inventive step in accordance with Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is maintained as granted.

The registrar:

The chair:

U. Bultmann

R. Moufang