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Datasheet for the decision of 31 January 2013

Case Number: T 0733/10 - 3.3.10

Application Number: 03718951.1

Publication Number: 1496951

IPC: A61L 15/38, A61F 13/15

Language of the proceedings: EN

Title of invention:
Wound dressings comprising an oxidoreductase enzyme in hydrated condition

Patent Proprietor:
Insense Limited

Opponent:
Flen Pharma N.V.

Headword:
Wound dressings/INSENSE

Relevant legal provisions:
EPC Art. 54, 56, 107

Keyword:
"Admissibility of patent proprietor's appeal (no), not adversely affected"
"Novelty (yes)"
"All requests: inventive step (no) - foreseeable improvement of oxygen delivery to wound"

Decisions cited:
T 0722/97

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0733/10 - 3.3.10

D E C I S I O N
of the Technical Board of Appeal 3.3.10
of 31 January 2013

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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 10 February 2010 concerning maintenance of the European patent No. 1496951 in amended form.**

Composition of the Board:

Chairman: P. Gryczka
Members: J. Mercey
C. Schmidt

Summary of Facts and Submissions

I. The Opponent and Patent Proprietor lodged appeals against the interlocutory decision of the Opposition Division which found that European patent No. 1 496 951 in amended form met the requirements of the EPC.

II. Notice of Opposition had been filed by the Opponent requesting revocation of the patent as granted in its entirety on the grounds of lack of novelty and inventive step (Article 100(a) EPC). *Inter alia* the following documents were submitted in opposition proceedings:

(1) WO-A-01 286 00,
(2) WO-A-99 655 38 and
(15) WO-A-91 111 05.

III. The decision under appeal was based on the patent as amended according to the only request pending at the end of the proceedings before the Opposition Division, said request having been filed during oral proceedings on 14 December 2009, all other requests having been withdrawn. Claim 2 of this request reads as follows:

"A skin dressing sealed in packaging, wherein the dressing comprises oxidoreductase enzyme in hydrated condition, and includes one or more cross-linked hydrated hydrogels and a source of substrate for the oxidoreductase enzyme, wherein the dressing is of layered construction and comprises an upper layer, remote from the skin in use, including the oxidoreductase enzyme and comprises a lower layer,

below the upper layer in use, including the source of substrate for the oxidoreductase enzyme."

IV. The Opposition Division held that the subject-matter of the claims of this only pending request fulfilled the requirements of Rule 80 and Article 123(2) EPC. It held that the subject-matter of independent claim 2 was novel over *inter alia* document (15), and involved an inventive step. Starting from Example 18 of document (15) as closest prior art, the Opposition Division considered that the problem to be solved by the invention was to prevent contact of the enzyme with the wound, prevent irritation and maximise delivery of oxygen to skin surface, and that this problem was solved in a non-obvious way by the subject-matter of claim 2 by virtue of the separation of the enzyme and the substrate in two layers.

V. With letter dated 8 June 2010, the Patent Proprietor filed a main request and auxiliary requests 1 to 5 and with letter dated 19 December 2012, it submitted auxiliary requests 6 to 8. During oral proceedings before the Board held on 31 January 2013, the Patent proprietor withdrew its main request and auxiliary requests 1 and 8.

Claim 2 of auxiliary request 2 and claim 1 of auxiliary request 3 are identical to claim 2 of the request maintained by the Opposition Division (see point III above).

Claim 1 of auxiliary request 4 differs from claim 2 of auxiliary request 2 in that the hydrated hydrogels are cross-linked.

Claim 1 of auxiliary request 5 differs from claim 1 of auxiliary request 4 in that the cross-linked hydrogel is further defined as being cross-linked sufficiently to form an entrapping biopolymer matrix that can retain the enzyme in the gel.

Claim 2 of auxiliary request 6 and claim 1 of auxiliary request 7 differ from claim 2 of auxiliary request 2 in that the upper layer is further defined as being in the form of an inert support and the lower layer as being in the form of a hydrated hydrogel.

VI. The Opponent argued that the Patent Proprietor's appeal was inadmissible, since the Proprietor was not adversely affected by the decision of the Opposition Division, its main request having been upheld thereby.

The Opponent submitted that the subject-matter of claim 2 of auxiliary request 2 was not novel over document (15), more particularly over the compositions disclosed therein in the form of two gels which maintained the glucose oxidase and D-glucose in separate phases.

The subject-matter of all claims relating to skin dressings of layered construction was not inventive in view of document (15) in combination with document (2), said latter document teaching wound dressings which were bilayer hydrogels wherein the hydrogel may be a cross-linked polyacrylate, Example 9 thereof describing a sandwich bilayer with glucose in a first hydrogel and glucose oxidase in a second hydrogel which was then exposed to water. Sealing such a composition for use in

a therapeutic application, such as wound healing, in packaging, belonged to the common general knowledge of the skilled person and was taught by document (15). The subject-matter of claim 1 of each of auxiliary requests 4 and 5 was also not inventive since document (1) taught the enzyme-entrapping effect of cross-linked hydrogels.

VII. With regard to the question of whether or not it had been adversely affected by the decision of the Opposition Division, the Patent Proprietor submitted that it did not remember having withdrawn the higher requests during the oral proceedings before the Opposition Division. It agreed that its appeal would be inadmissible were this the case, it having contested neither the correctness of the minutes of the oral proceedings before the Opposition Division, nor the correctness of the contested decision.

The Patent Proprietor argued that the subject-matter of claim 2 of auxiliary request 2 was novel over document (15), since said document did not disclose a skin dressing of layered construction, nor a hydrated hydrogel, let alone such a dressing sealed in packaging.

The subject-matter of all claims relating to skin dressings of layered construction was inventive, since the skilled person would not have packaged the bilayer membrane of document (2) in a hydrated condition, document (15) teaching away from storing the compositions disclosed therein in the presence of water. The subject-matter of claim 1 of each of auxiliary requests 4 and 5 was additionally inventive in view of

the hydrogel being cross-linked which entrapped the enzyme, thus preventing its release into the wound bed during use. Although this effect was already taught by document (1), the wound dressings of said document contained no substrate for the enzyme. In any case, the skilled person would not have used a cross-linked hydrogel in the compositions of document (15) as these required swift release of the enzyme prior to use.

VIII. The Opponent requested that the decision under appeal be set aside and that the patent be revoked.

The Patent Proprietor requested that the decision under appeal be set aside and the patent be maintained on the basis of any of auxiliary requests 2 to 5 filed with letter dated 8 June 2010, or on the basis of auxiliary requests 6 or 7, filed with letter dated 19 December 2012.

IX. At the end of the oral proceedings, the decision of the Board was announced.

Reasons for the Decision

1. *Admissibility*

1.1 The admissibility of the Opponent's appeal was not challenged, the appeal indeed being clearly admissible. The Opponent will thus hereinafter be referred to as the Appellant.

1.2 In contrast, the admissibility of the Patent Proprietor's appeal has been challenged by the

Appellant for not fulfilling the requirements of Article 107 EPC, the Patent Proprietor not having been adversely affected by the decision of the Opposition Division.

1.2.1 The decision of the Opposition Division to maintain the patent in amended form is based on the sole version proposed by the Patent Proprietor, namely the request filed during the oral proceedings before the Opposition Division which, following withdrawal of all other requests, became its main and sole request. As the decision follows its request, the Patent Proprietor is not adversely affected and as such, an appeal filed by the Proprietor must be considered as inadmissible (see T 722/97, not published in OJ EPO).

1.2.2 This conclusion was not contested by the Patent Proprietor, which merely submitted that it did not remember having withdrawn the higher requests during the oral proceedings before the Opposition Division. However, the minutes of said proceedings and the wording of the contested decision are quite clear and unambiguous in this respect, the penultimate paragraph of the minutes and point 2.11 of the decision indicating that a new request was filed during said oral proceedings, which was the **only** request on file, as **all other requests were withdrawn** (emphasis added). The Patent Proprietor never contested the correctness of either the minutes or the decision.

1.2.3 In view of the above, the Patent Proprietor's appeal has to be rejected as inadmissible (Article 107 EPC, first sentence; Rule 101(1) EPC). The Patent Proprietor will thus hereinafter be referred to as the Respondent.

2. *Requests on file*

During the oral proceedings before the Board, the Respondent withdrew its main request and auxiliary requests 1 and 8. This decision is thus based on auxiliary requests 2 to 7 only. Auxiliary requests 2 and 6 contain two independent claims, auxiliary requests 3 to 5 and 7, only one. Since all of the requests contain an independent claim directed to a skin dressing of layered construction, namely claim 2 of auxiliary requests 2 and 6 and claim 1 of auxiliary requests 3 to 5 and 7, it is appropriate that the patentability of the subject-matter of these claims is examined first.

Auxiliary request 2

3. *Novelty*

3.1 The Appellant challenged the novelty of the subject-matter of claim 2 of auxiliary request 2 with regard to document (15).

3.2 Document (15) discloses compositions which may provide the active component of a product including impregnated materials such as wound dressings (see page 10, lines 30 to 34 and page 11, line 18). Said compositions may be provided in the form of two physically separated phases in which the glucose oxidase is prevented from coming into contact with D-glucose until immediately prior to use, for example, they may take the form of two gels which maintain the glucose oxidase and D-

glucose in separate phases until the two are physically combined prior to use (see page 8, lines 16 to 24).

3.3 However, document (15) does not disclose a skin dressing of layered construction including a hydrated hydrogel. Thus, neither of the two gel phases disclosed on page 8, line 22 is described as being hydrated. Furthermore, the compositions taking the form of two gel phases referred to on page 8, line 22 are not necessarily of layered construction, since two gel phases may take the form of an emulsion, for example, as in Example 18 of document (15). In any case, a skin dressing comprising two gel phases is not unambiguously disclosed, since these two gel phases are "combined prior to use". Thus, said compositions taking the form of two gels are, for example, first dissolved or vigorously mixed (see page 8, lines 24 to 29), i.e. diluted and activated whereupon the glucose oxidase and D-glucose are brought into intimate admixture (see page 7, lines 14 to 20). As a result, the two gel phases would no longer separately exist once the composition was used to impregnate a material in order to make a wound dressing. Since document (15) does not disclose a skin dressing of layered construction including a hydrated hydrogel, then it also cannot disclose such a dressing sealed in packaging.

3.3.1 The Appellant argued that it was implicit that the gels described at page 8, line 22 were hydrated, since they would not otherwise need to be separated in order to prevent the glucose oxidase and D-glucose from reacting.

However, the paragraph of document (15) on page 8, lines 16 to 29 also describes the physical separation

of the glucose oxidase and D-glucose in the form of two powders and/or as a double layer tablet which is dissolved prior to use. Thus, said paragraph envisages the separation of glucose oxidase and D-glucose even when in dry form, such that it is not implicit that the gels disclosed therein are hydrated.

3.3.2 The Appellant also argued that document (15) did not necessarily describe that the compositions disclosed therein were always diluted and activated prior to their use in a product. Thus, according to page 9, lines 4 to 7, the compositions of the invention were incorporated as preservatives into formulations for topical application; page 10, lines 18 to 28 disclosed that the preserved compositions included cosmetic products, toiletries and pharmaceutical preparations *per se*; and page 14, lines 1 to 4 indicated that the concentrated compositions might be diluted for either active or preservative use.

However, the passage at page 8, lines 16 to 29 on which the Appellant bases its novelty objection specifically states that the glucose oxidase and D-glucose are maintained in two separate phases until the two are **physically combined prior to use** (emphasis added). Hence, when such a composition is used to impregnate a material to form a wound dressing, the glucose and D-glucose are first brought into contact which means that the two separate gel phases would no longer necessarily exist.

3.4 Thus, since no skin dressings of layered construction including a hydrated hydrogel are directly and unambiguously disclosed in document (15), the subject-

matter of claim 2 is novel (Article 54 EPC) over the disclosure of this document.

4. *Inventive step*

4.1 Claim 2 is directed to a dressing of layered construction comprising hydrated oxidoreductase enzyme in one layer and a source of substrate for said enzyme in the other layer. Document (15) discloses wound dressings comprising glucose oxidase and D-glucose (see page 1, lines 2 to 5 and page 11, line 18).

4.1.1 The Board considers, in agreement with the Opposition Division, the Appellant and the Respondent, that the wound dressing of document (15) represents the closest state of the art and, hence, takes it as the starting point when assessing inventive step.

4.2 In view of this state of the art, the problem underlying the patent in suit as formulated by the Respondent and indicated in paragraph [0054] of the specification of the patent in suit consists of the provision of a wound dressing which more efficiently delivers oxygen from the ambient atmosphere outside the wound into the wound bed.

4.3 As the solution to this problem, claim 2 of auxiliary request 2 proposes a dressing of layered construction comprising hydrated oxidoreductase enzyme in one layer and a source of substrate for said enzyme in the other layer.

4.4 The Respondent explained that oxygen delivery to the wound was improved because the oxidoreductase enzyme

was present in an upper layer of the dressing, such that on application of the dressing to the skin, said enzyme was closer to the atmosphere, thus enhancing the uptake of oxygen therefrom. In addition, in view of the presence of a lower layer, the enzyme was not in contact with the skin, such that it was less able to take oxygen from the wound. The Board holds that said explanation is credible, such that even without experimental evidence it is plausible that the technical problem as defined above in point 4.2 is solved by the claimed skin dressing.

4.4.1 The Appellant argued that the objective problem to be solved by the patent in suit was merely the provision of an alternative skin dressing, since enzyme would clearly diffuse into the lower layer rendering it remoter from the atmosphere and closer to the wound, such that improved oxygen transport was no longer plausible.

However, even if enzyme may indeed diffuse into the lower layer, this process takes time and would merely decrease the desired effect but not entirely remove it, particularly in the typically short time periods for which a skin dressing is used. This argument must thus be rejected.

4.5 Finally, it remains to be decided whether or not the proposed solution to the problem underlying the patent in suit involves an inventive step in view of the state of the art.

4.5.1 When starting from the wound dressings known from document (15), it is a matter of course that the person

skilled in the art seeking to provide improved skin dressings would turn his attention to that prior art addressing other wound dressings comprising substrate oxidoreductases, for example, document (2) which discloses wound dressings comprising glucose and glucose oxidase encapsulated as dry solids in a polymer base (see page 9, line 12, page 28, lines 19 to 20 and page 46, lines 19 to 22). More particularly, Example 9 of said document discloses lyophilised hydrogels of glucose and glucose oxidase in separate membranes which are placed one on top of one other and pressed to form a bilayer sandwich which is then cut into various shapes. This bilayer membrane is then exposed to water which presumably leads to hydration of the glucose oxidase and hydrogel.

The skilled person would thus be taught by document (2) that the dressing may have a layered structure comprising a layer including the glucose oxidase enzyme and another layer including the substrate therefor, namely glucose. It is implicit from the structure of this dressing, that one layer may be placed next to the skin and the other closer to the atmosphere such that efficient oxygen delivery to the wound was implicit and foreseeable (see point 4.4 above). Sealing said dressing in packaging with the glucose oxidase and hydrogel in hydrated condition cannot be seen to involve any inventive ingenuity, since document (15) itself teaches that concentrated water-containing compositions including glucose oxidase and glucose may be packaged and maintained prior to use under substantially anaerobic conditions (see page 8, lines 8 to 11).

4.6 The Respondent argued that the skilled person would not have packaged the bilayer membrane of document (2) in a hydrated condition, since document (15) taught away from storing the compositions disclosed therein in the presence of water, since it proposed the physical separation of the enzyme from at least one of its substrates, for example, water, in order to prevent the production of hydrogen peroxide during storage (see page 6, lines 31 to 35).

However, as stated in point 4.5.1 above, document (15) also teaches that water-containing compositions may be packaged so long as this is under substantially anaerobic conditions. Such compositions may indeed be less stable than those containing no water, but the Respondent has not shown that its claimed skin dressings exhibit surprising stability.

4.7 As a result, the subject-matter of claim 2 is obvious to the skilled person in view of the combination of the teachings of documents (15) and (2). The Respondent's auxiliary request 2 is thus not allowable for lack of inventive step pursuant to Article 56 EPC.

Auxiliary request 3

5. Claim 1 of auxiliary request 3 is identical to claim 2 of auxiliary request 2, such that this request is also not allowable for lack of inventive step pursuant to Article 56 EPC.

Auxiliary requests 4 to 7

6. *Novelty*

Claim 1 of auxiliary requests 4, 5 and 7 and claim 2 of auxiliary request 6 comprise more features than claim 2 of auxiliary request 2 such that the subject-matter of each of these claims is also novel for at least the same reasons as those given for claim 2 of auxiliary request 2 (see point 3 above).

Auxiliary request 4

7. *Inventive step*

7.1 Claim 1 of auxiliary request 4 differs from claim 2 of auxiliary request 2 in that the dressing comprises one or more cross-linked hydrated hydrogels.

7.2 Document (2), however, already teaches that the hydrogel is preferably a cross-linked polyacrylate (see page 17, lines 22 to 24). Even if the technical problem underlying the invention is now additionally defined as maintaining the enzymes in the gel, thus preventing release of the enzyme into the wound bed, the entrapment of oxidoreductase enzyme by cross-linked gels in wound dressings is already taught by document (1) (see page 9, lines 27 to 32). Thus this amendment cannot contribute to inventiveness of the subject-matter of claim 1 of auxiliary request 4 *vis-à-vis* this document.

7.3 The Respondent argued that the skilled person would not have incorporated a cross-linked gel into the

compositions according to document (15) as these required swift release of the enzyme upon intimate admixture of the concentrated compositions with water when using them to impregnate wound dressings, which was at odds with the use of a cross-linked gel which was known to entrap the enzyme. The physical separation of the enzyme from the substrate was described in this document merely for the purpose of storage of the concentrated compositions. In any case, the teaching of document (15) was not compatible with the teaching of document (2), since document (2) did not disclose packaged wound dressings in hydrated condition, nor with that of document (1), since the wound dressings disclosed therein contained no substrate for the enzyme.

However, it is irrelevant that the dressings of document (1) do not contain a substrate for the enzyme, since said feature is already taught by both documents (2) and (15). Likewise, just because document (2) does not describe the packaging of hydrated dressings, does not render this teaching incompatible with that of document (15), since document (15) teaches the storage of both anhydrous and water-containing compositions (see page 7, line 30 to page 8, line 15). With regard to the Respondent's argument that the skilled person would not have used a cross-linked hydrogel in the wound dressings of document (15) in view of the fact that the two-phase gel compositions described therein required quick release of the enzyme once they were physically combined, the Board holds that on combining the teachings of documents (15) and (2), the skilled person is aware that the structures of the dressings described in document (2) are not intended to be destroyed prior to use and would thus incorporate the

bilayer sandwich structure intact into the teaching of document (15).

7.4 Therefore, the considerations having regard to the assessment of inventive step given in points 4.1 to 4.6 above and the conclusion drawn in point 4.7 above with respect to claim 2 of auxiliary request 2 apply also to claim 1 of auxiliary request 4.

7.5 Thus, auxiliary request 4 is also not allowable for lack of inventive step pursuant to Article 56 EPC.

Auxiliary request 5

8. *Inventive step*

8.1 Claim 1 of auxiliary request 5 differs from claim 1 of auxiliary request 4 in that the cross-linked hydrogel is further defined as cross-linked sufficiently to form an entrapping biopolymer matrix that can retain the enzyme in the gel.

8.2 However, this additional definition of the cross-linked hydrogel does not alter the assessment of inventive step made above for the subject-matter of auxiliary request 4, since the Board accepts that the term "cross-linked" alone already implies that the enzyme is retained, at least to some extent, in the gel.

8.3 Thus, auxiliary request 5 is also not allowable for lack of inventive step pursuant to Article 56 EPC.

Auxiliary request 6

9. *Inventive step*

9.1 Claim 2 of auxiliary request 6 differs from claim 2 of auxiliary request 2 in that the upper layer of the dressing is further defined as being in the form of an inert support and the lower layer as being in the form of a hydrated hydrogel.

9.2 However, Example 9 of document (2) already describes a wound dressing comprising a lower layer in the form of a hydrogel containing glucose (see point 4.5.1 above). The upper layer of the bilayer membrane of Example 9 is also a hydrogel which, in the absence in present claim 2 of any further definition of the term "inert", may be considered to be an inert support. Thus these amendments cannot contribute to inventiveness of the subject-matter of claim 1 of auxiliary request 6 *vis-à-vis* this document, the Respondent not providing any further arguments in support of inventive step for the subject-matter of this request.

9.3 Thus, auxiliary request 6 is also not allowable for lack of inventive step pursuant to Article 56 EPC.

Auxiliary request 7

10. Claim 1 of auxiliary request 7 is identical to claim 2 of auxiliary request 6, such that this request is also not allowable for lack of inventive step pursuant to Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

C. Rodríguez Rodríguez P. Gryczka