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Datasheet for the decision of 22 February 2010

Case Number: T 0444/07 - 3.3.02

Application Number: 97905534.0

Publication Number: 0914093

IPC: A61K 9/08

Language of the proceedings: EN

Title of invention:
Use of a solution comprising glucose for peritoneal dialysis having reduced formation of age products

Patentee:
Gambro Lundia AB

Opponent:
Baxter Healthcare Corpn

Headword:
Peritoneal dialysis/GAMBRO LLUNDIA AG

Relevant legal provisions:
EPC Art. 56

Relevant legal provisions (EPC 1973):
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Keyword:
"Main, first, second requests - inventive step - no: obvious in the light of the chemical similarity"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0444/07 **-** 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 22 February 2010

Appellant: (Opponent)
Baxter Healthcare Corpn
One Baxter Parkway
Deerfield
Illinois 60015 (US)

Representative:
Crowhurst, Charlotte Waveney
Potter Clarkson LLP
Park View House
58 The Ropewalk
Nottingham NG1 5DD (GB)

Respondent: (Patent Proprietor)
Gambro Lundia AB
Box 10101
S-220 10 Lund (SE)

Representative:
Simons, Amanda Louise
J.A. Kemp & Co.
14 South Square
Gray's Inn
London WC1R 5JJ (GB)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 11 January 2007 rejecting the opposition filed against European patent No. 0914093 pursuant to Article 102(2) EPC.**

Composition of the Board:

Chairman: U. Oswald
Members: J. Riolo
J. Van Moer

Summary of Facts and Submissions

I. European patent No. 0 914 093, based on European application No. 97 905 534.0, was granted on the basis of 6 claims.

Independent use claim 1 as granted read as follows:

1. Use of a solution comprising glucose, in which the glucose portion is sterilised separately from the remaining components at a high glucose concentration above about 20% and mixed with the remaining components after sterilisation, for the preparation of a peritoneal solution having reduced formation of advanced glycosylation end products for the treatment of diseases related to advanced glycosylation products.

Independent process claim 4 as granted read as follows:

4. Process for the prevention of the formation of advanced glycosylation end products in solution for peritoneal dialysis that comprise glucose, characterized in that the glucose portion is sterilised separately from the remaining components at a high glucose concentration above about 20% and mixed with the remaining components after sterilization.

II. Opposition was filed against the patent under Article 100(a) EPC for lack of novelty and inventive step, Article 100(b) EPC for insufficiency of disclosure.

The following documents ***inter alia*** were cited during the proceedings before the Opposition Division and the Board of Appeal:

(1) WO93/09820
(10) "In Vitro Biocompatibility of a Heat-Sterilized, Low-Toxic, and Less Acidic Fluid for Peritoneal Dialysis", Wieslander et al., Peritoneal Dialysis International, 15, pp 158-164, 1995
(15) Lamb et al., Kidney Int., 47, pp 1768-1774, 1995

III. By its decision pronounced on 15 November 2006, the Opposition Division rejected the opposition under Article 102(2) EPC.

The notice of opposition requested the revocation of the patent in suit in its entirety on the basis of Article 100(a) EPC (lack of novelty and inventive step) and on the basis of Article 100(b) EPC (insufficiency of the description of the invention).

As to Article 100(b) EPC, contrary to the opponent's view, the Opposition Division did not consider that the skilled person would not know from the patent how to use the peritoneal dialysis solutions of the patent in suit to produce a medicament that could be used to treat diseases related to Advanced Glycolsylation End Products (AGE).

In its opinion, using such peritoneal dialysis solutions was a matter of routine, and that the diseases which were intended for treatment were also well known. Moreover, as the preparation of the peritoneal dialysis itself was concerned, the

Opposition Division also considered that the specification of the contested patent provided sufficient information for it to be reproduced by a person of ordinary skill. Indeed, the part "detailed description of the invention" provided sufficient experimental data to illustrate the preparation of such a solution having less GDP and causing less formation of the AGE pyrraline. It followed that the Opposition Division came to the conclusion that the requirements of Article 100(b) EPC were met.

Concerning the novelty of independent claims 1 and 4 of the contested patent over document (1), the Opposition Division concluded that neither subject-matters were anticipated for the following reasons:

Document (1) disclosed a process for the preparation of peritoneal dialysis solutions wherein the glucose portion was sterilised separately from the remaining components at a high glucose concentration above about 20% and mixed with the remaining components after sterilisation. That document mentioned that the process allowed to reduce the formation of GDP (glucose degradation products). However, it did neither explicitly nor implicitly mention AGE (Advanced Glycosylation End products).

Independent claim 1 was accordingly novel since it related to the treatment of diseases related to advanced glycosylation products and independent claim 4 because it concerned a process for the prevention of the formation of advanced glycosylation end products in a solution of peritoneal dialysis that comprises glucose.

Finally, as regards inventive step, the Opposition Division considered that the problem at the basis of the present invention was the provision of a solution for peritoneal dialysis, which prevents the formation of AGE products, as indicated on paragraph 1 of the contested patent. Such peritoneal dialysis solutions would then be particularly suitable for the dialysis treatment of patients suffering from AGE-related diseases.

The Opposition Division considered that the closest prior art was represented by document (15). That document addressed the problem at the basis of the invention, namely the formation of AGE products in peritoneal dialysis fluids comprising glucose. That document also proposed a solution to that problem, which consisted in the incorporation of inhibitors of the Maillard reaction, such as aminoguanidine, in the dialysis fluid.

Thus, in light of this document, the new objective problem could be seen as the provision of an alternative solution for the prevention of the formation of AGE products in peritoneal dialysis fluids.

Document (l), which disclosed a process for the heat sterilisation of glucose-containing peritoneal dialysis solutions, wherein lower degradation of glucose during the heat sterilisation was achieved by separating the glucose from the other components during the heat sterilisation step, did not teach the solution at the

basis of the invention as it is totally silent about AGE product formation.
Accordingly, the Opposition Division concluded that the subject-matter of the main request involved an inventive step in the sense of Article 56 EPC.

The above reasoning was considered to be also valid for both independent use claim 1 and independent process claim 4, as well as to the claims dependent thereof.

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

V. In a communication from the Board dated 5 February 2010, the Board expressed its preliminary opinion that the subject-matter of independent claim 1 of the patent in suit seemed not to involve an inventive step vis-à-vis documents (10) and (15) in combination and that the subject-matter of independent claim 4 was anticipated by the disclosure in document (1).

VI. With a letter dated 17 February 2010, the respondent (patent proprietor informed the Board that the Board of Appeal's provisional opinion, which was sent to the appellant on 5 February, had just come to its attention.

VII. The Board of appeal communication of 5 February 2010 was faxed to the respondent on 19 February 2010.

VIII. Oral proceedings were held before the Board on 22 February 2010.

At the beginning of the oral proceedings, the respondent was invited to indicate whether it requested

the postponement of oral proceedings having regard to its letter dated 17 February 2010.
The respondent indicated that it agreed that the oral proceedings be held.

It filed a main and two auxiliary requests at the beginning of the oral proceedings.

The parties were first invited to put forward their submissions as to inventive step since the Board had already expressed its preliminary negative view in that respect.

IX. During the oral proceedings, the appellant essentially agreed with Board's preliminary opinion as to inventive step, that is, that documents destined to be read by specialised and expert people do represent the basic technical knowledge of a skilled person and can therefore be used to establish a link between prior art documents, so that the combination of document (15) and document (10) rendered the claimed subject-matter obvious.

Starting from document (10), the problem to be solved by the subject invention is defined as the provision of a new use of the peritoneal dialysis solution described in said document.

This document taught that the solutions used in the present invention contain lower levels of breakdown products of glucose, such as methylglyoxal, than solutions made by conventional methods.

Document (15) disclosed that there were probably potential "factors" in dialysate, which could be responsible for AGE formation. It moreover mentioned 3-deoxyglucosone, a breakdown product of glucose, known as a potential reactant in the late stages of the Maillard reaction leading to AGE formation.

Having regard to the structural and chemical similarity between 3-deoxyglucosone and methylglyoxal, the skilled person would consider methylglyoxal as a one of the potential "factors" in dialysate leading to AGE formation.

It would therefore be obvious to the skilled person that the use of such a solution in peritoneal dialysis could reduce AGE formation, and thus complications associated with AGE formation.

X. The respondent mainly argued during the oral proceedings that the skilled person would not combine documents (10) and (15) because the field of peritoneal dialysis was a very restricted research area involving few people and because these documents dealt with different aspects, namely document (10) was concerned with the chemistry in dialysis solutions and document (15) with clinical aspects.

XI. The appellant requested that the decision under appeal be set aside and that the patent be revoked.

The respondent requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or first, or second auxiliary requests submitted during the oral proceedings.

Reasons for the decision

1. The appeal is admissible.

2. Admissibility of the main and auxiliary requests filed during the oral proceedings.

The main request corresponds to the set of claims as granted wherein the process claims were deleted in direct reply to the novelty objection raised in the Board communication.

Independent claim 1 of the first auxiliary request corresponds to independent claim 1 of the set of claims of auxiliary request 2 filed in reply to the statement of the grounds of appeal, wherein the process claims were deleted and wherein the wording "diseases related to advanced glycosylation products" has been reintroduced in order to cope with the objection under Article 123(3) EPC raised by the appellant with respect of the deletion of this feature.

It reads:

1. Use of a solution comprising glucose, in which the glucose portion is sterilised separately from the remaining components at a high glucose concentration above about 20% and mixed with the remaining components after sterilisation, for the preparation of a peritoneal solution having reduced formation of advanced glycosylation end products for the treatment of diseases related to advanced glycosylation products,

chosen from tissue disorders which are vascular damage, dyslipidaemia and β-2-microglobuline amyloidosis.

Independent claim 1 of the second auxiliary request corresponds to independent claim 1 of the set of claims of auxiliary request 3 filed in reply to the statement of the grounds of appeal wherein the process claims were deleted.

It reads:

1. Use of a solution comprising glucose, in which the glucose portion is sterilised separately from the remaining components at a high glucose concentration above about 20% and mixed with the remaining components after sterilisation, for the preparation of a peritoneal solution having reduced formation of advanced glycosylation end products for the treatment of diseases related to advanced glycosylation products, in diabetic patients.

Accordingly, these requests are admitted into the proceedings.

3. Main request

Preliminary remark

In its written submissions, the appellant provided a discussion of the clarity and interpretation of claim 1. However, as pointed out by the respondent, it should be noted that the clarity of the claim is not in question as Article 84 cannot be raised during Opposition Proceedings against the granted claims.

3.1 Article 100(b) EPC

The Board agrees with the Opposition Division's favourable conclusions as to Article 100(b) EPC.

Having regard to the Board's conclusions in the assessment of inventive step (see below, point 3.3) and to the fact that the appellant did not put forward new arguments compared with those submitted and dealt with before the Opposition division, there would appear to be no need to devote further attention to this issue.

Accordingly, the Board concludes that the subject-matter of the main request fulfils the requirements of Article 100(b) EPC (see above under III, and the Opposition Division's decision, point 2.1).

3.2 Novelty

The Board agrees with the Opposition Division's favourable conclusions regarding Article 54 EPC with respect to this subject-matter.

Having regard to the Board's conclusions in the assessment of inventive step (see below, point 3.3) and to the fact that the appellant did not put forward new arguments compared with those submitted and dealt with before the Opposition division, there would appear to be no need to devote further attention to this issue.

Accordingly, the Board concludes that the subject-matter of the main request fulfils the requirements of

Article 54 EPC (see above under III, and the Opposition Division's decision, point 2.2).

3.3 Inventive step

3.3.1 The contested patent relates to the use of a peritoneal solution comprising glucose, in which the glucose portion is sterilised separately from the remaining components at a high glucose concentration above about 20% and mixed with the remaining components after sterilisation. This peritoneal solution reduces the formation of advanced glycosylation end products. It is therefore indicated for patients suffering from diseases related to advanced glycosylation products (claim 1, paragraphs 4 to 7 and 11 and 12).

Document (15), which is cited in the patent in suit in paragraph 8, is an article investigating the ***in vitro*** formation of advanced glycation end products in peritoneal dialysis fluid.

The Board agrees with the respondent that document (15) could be regarded as the closest prior art.

Document (15) investigates peritoneal dialysis solutions of conventional composition in which all components are heat-sterilised together as a single solution. The article states that late Maillard reaction products (i.e. non-enzymatic reaction between proteins and sugar or degradation products thereof producing highly insoluble, fluorescent, pigmented inter-molecular cross-linked polymers) are formed to a higher extent in conventional peritoneal dialysis solutions. Moreover, the article concludes that such

AGE product formation is greater in fresh dialysis fluid. The article further concludes that results suggest that conventional peritoneal dialysis fluid may contain a factor (or factors) which promotes AGE product formation and that it may be possible to include inhibitors, such as aminoguanidine, n the dialysis fluid (summary, page 1768, first paragraph, left column; page 1771, right column, third paragraph; page 1772, paragraph bridging left and right columns; page 1773, paragraph bridging left and right columns).

3.3.2 The problem to be solved by the subject-matter of claim 1 of the main request of the patent in suit as against document (15) can be seen in the provision of a means for reducing AGE product formation in peritoneal dialysis.

3.3.3 This problem is solved by using a peritoneal solution comprising glucose, in which the glucose portion is sterilised separately from the remaining components at a high glucose concentration above about 20% and mixed with the remaining components after sterilisation.

In the light of the description and examples in the patent in suit, and in the absence of any specific evidence to the contrary, the Board is satisfied that the problem has been solved.

3.3.4 Thus the question to be answered is whether the proposed solution would have been obvious to the skilled person in the light of the prior art.

In that respect, the Board observes that document (15) envisages the possibility of including inhibitors of

the Maillard reaction, such as aminoguanidine, in the dialysis fluid.

It is however silent about any particular measure regarding the preparation process for the peritoneal solutions.

Document (15) moreover discloses that 3-deoxyglucosone ($CHO-CO-CO-CH_2-CHOH-CHOH-CH_2OH$) has been found as a spontaneous breakdown product of glucose in dialysate and that it is a potential reactant in the late stages of the Maillard reaction.

Document (10) describes a study that was conducted using a peritoneal dialysis solution that was produced by using the method recited in claim 1 of the subject patent (paragraph under the heading "Test PD Fluids" on page 159).

This document compares the level of certain glucose degradation products in peritoneal dialysis solutions produced by "conventional" methods and produced by a method which is the same as the method recited in subject claim 1.

The results reported in document (10) show that this solution is a peritoneal dialysis solution in which the amount of methylglyoxal ($CHO-CO-CO-CH_3$)is greatly reduced by use of the method recited in subject claim 1 (in Table 2).

Thus, it explicitly discloses that producing a peritoneal dialysis solution using the method defined

in claim 1 of the subject patent will reduce the amount of methylglyoxal.

Having regard to the structural and chemical similarity between 3-deoxyglucosone and methylglyoxal (i.e. **CHO-CO-CO-CH_2**-CHOH-CHOH-CH_2OH/**CHO-CO-CO-CH_3**), the skilled person would consider methylglyoxal also as a one of the potential "factors" in dialysate leading to AGE formation, as is the case for 3-deoxyglucosone since they share an identical reactive moiety.

The Board has no doubt that the skilled person is well aware of the disclosures in (10) and (15), since, as is apparent from the review titles (Peritoneal Dialysis International and Kidney International), they are both relevant to the technical field of dialysis.

Accordingly, the Board is convinced that the skilled person, faced with the problem defined under 3.3.2, would have considered the peritoneal solution disclosed in document (10).

3.3.5 The Board does not agree with the respondent's main lines of argument that the skilled person would not combine document (10) and (15) because the field of peritoneal dialysis was a very restricted research area involving few people and because these documents dealt with different aspects, namely document (10) was concerned with the chemistry in dialysis solutions and document (15) with clinical aspects.

Indeed, as explained above, both documents relate in fact to dialysis, as already apparent from the titles

of the articles (i.e. Peritoneal Dialysis International and Kidney International).
Moreover, the chemical aspects in document (10) relate to a very simple chemical structure, namely sugar and degradation products thereof.
Nor is it correct that document (15) is not concerned with chemistry since it mentions the chemical reaction involved in the Maillard reaction and chemical structures such as 3-deoxyglucosone.
Under these circumstances, it can only be concluded that the skilled person in the field of dialysis must have some basic knowledge of chemistry.

As to the argument relating to the fact that there is only a small community involved in the field of dialysis, the Board sees that rather as an indication that its members would be well informed of the work done by the various research groups in this field.

3.3.6 In the light of these facts, the Board can only conclude that the subject-matter of claim 1 of the main request does not involve an inventive step as required by Article 56 EPC.

Under these circumstances, there is no need to consider the remaining claims.

4. Auxiliary requests 1 and 2

During the oral proceedings, both parties agreed that the auxiliary requests, which, as indicated by the respondent during the oral proceedings, were primarily deemed, if needed, to establish novelty, did not add anything new in relation to the assessment of inventive

step, and therefore merely referred to their submissions as to the main request.

Thus, as there are no additional distinguishing features in these requests which appear to be non-obvious vis-à-vis the combination of documents (10) and (15), the conclusion as to lack of inventive step for the subject-matter of claim 1 of the main request applies equally to these requests, as it appears from the above that it was obvious to specifically use the peritoneal dialysis solution according to the patent in suit with any patients suffering from any diseases related to advanced glycosylation products.

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

N. Maslin U. Oswald