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D E C I S I O N
of 29 June 2006

Case Number: T 0251/02 - 3.3.02

Application Number: 86905644.0

Publication Number: 0238553

IPC: A61K 31/16

Language of the proceedings: EN

Title of invention:
Method of treating catabolic dysfunction

Patentee:
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Opponent:
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SCIENTIFIC HOSPITAL SUPPLIES INTERNATIONAL LIMITED
FRESENIUS AG
N.V. Nutricia

Headword:
Catabolic dysfunction/THE BRIGHAM AND WOMEN'S HOSPITAL, INC.

Relevant legal provisions:
EPC Art. 56

Keyword:
"Main and auxiliary requests 1 to 5 - inventive step - no: obvious combination of two documents to verify a suggested novel technical effect"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0251/02 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 29 June 2006

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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 21 January 2002 revoking European patent No. 0238553 pursuant to Article 102(1) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: J. Riolo
J. Willems

Summary of Facts and Submissions

I. European patent No. 0 238 553, based on international application No. PCT/US86/01870, was granted on the basis of 7 claims.

Independent claim 1 as granted read as follows:

"1. The use of glutamine or a functional analogue thereof that retains the characteristics of glutamine in the preparation of an agent for treating atrophy of small intestinal mucosa, the atrophy caused by catabolic dysfunction."

Dependent claims 4 and 5 read as follows:

"4. The use as claimed in claim 1 or 2, wherein the atrophy occurs subsequent to physical trauma."

"5. The use as claimed in claim 4, wherein the physical trauma is associated with surgery, sepsis, burn injuries, anorexia, chemotherapy, radiation therapy or uncontrolled diabetes."

II. Oppositions were filed against the granted patent by opponents O1 to O4. The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step and because it lacked industrial applicability under Article 52(4) EPC, for insufficiency of disclosure under Article 100(b) EPC and because the subject-matter of the European patent extended beyond the content of the application as filed under Article 100(c) EPC.

With its letter dated 27 April 1999, opponent O3 withdrew its opposition.

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

(E1) Journal of Parenteral and Enteral Nutrition, Vol. 9, No. 1, pages 18-22, January/February 1985
(51) General Product Information Sheet for "Vivonex HN": Norwich Eaton Ltd, March 1985
(D9) EP-A-87 750

III. By its decision pronounced on 29 May 2001, the Opposition Division revoked the patent under Article 102(1),(3) EPC.

The Opposition Division held that neither the set of claims of the main request nor the sets of claims of auxiliary requests 1 and 3 met the requirements of the EPC.

The Opposition Division considered that the requirements under Article 100(b) EPC were fulfilled because, contrary to the view of the opponents, the terms "atrophy caused by catabolic dysfunctions" were sufficiently disclosed in the patent in suit and because the other objections raised by the opponents with regard to this article were in fact a matter of Article 84 EPC, which was not a ground for opposition.

It also concluded that the subject-matter of the contested patent was present in the priority document, so that the priority was validly claimed.

It was further of the opinion that the claims were correctly drafted as "second medical use" claims. The objection raised under Article 54(2) EPC was therefore deemed to be ill-founded.

The main request (set of claims as granted) was rejected by the Opposition Division because the subject-matter of dependent claims 4 and 5 was not disclosed in the application as originally filed. It held however that the subject-matter of claim 1 and dependent claims 3 met the requirements of Article 123(2) EPC in the light of the disclosure in various parts of the application as originally filed, which it referred to in the text of the decision.

As to novelty, the Opposition Division held that none of the documents disclosed the specific use of glutamine *per se* according to the contested patent, ie for treating the atrophy of small intestine mucosa.

The Opposition Division considered however that this second medical application was obvious in the light of document (E1), which suggested the use of exogenous glutamine for treating villus atrophy.

Auxiliary requests 1 and 3 were therefore rejected for lack of inventive step. Dependent claims 4 and 5 were deleted from these requests.

Auxiliary request 2 was not admitted into the proceedings since it has been filed late.

Accordingly, the Opposition Division revoked the patent in suit.

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

V. Oral proceedings were held before the Board on 29 June 2006.

The appellant filed one main and five auxiliary requests during the appeal proceedings with its letter dated 28 May 2002.

Dependent claims 4 and 5 as granted were deleted in all requests.

As regards the remaining claims, the set of claims of the main request corresponds to the set of claims as granted.

Claim 1 of the first auxiliary request reads:
"1. The use of glutamine or a functional analogue thereof that retains the characteristics of glutamine in the preparation of an agent for treating atrophy of small intestinal mucosa, the atrophy caused by catabolic dysfunction, wherein **administration of a therapeutically effective amount of the glutamine or analogue thereof is parenteral**." (emphasis added).

Claim 1 of the second auxiliary request reads:
"1. The use of glutamine or a functional analogue thereof that retains the characteristics of glutamine in the preparation of an agent for treating atrophy of small intestinal mucosa, the atrophy caused by

catabolic dysfunction, wherein **administration of a therapeutically effective amount of the glutamine or analogue thereof is intravenous** and **wherein the therapeutically effective amount is greater than or equal to 0.1 grams per kg of body weight per day**." (emphasis added).

Claim 1 of the third auxiliary request reads:
"1. The use of glutamine or a functional analogue thereof that retains the characteristics of glutamine in the preparation of an agent for treating atrophy of small intestinal mucosa, the atrophy caused by catabolic dysfunction, **wherein the atrophy of intestinal mucosa that occurs is substantially associated with intravenous feeding**." (emphasis added).

Claim 1 of the fourth auxiliary request is identical to claim 1 of the second auxiliary request.

Claim 1 of the fifth auxiliary request reads:
"1. The use of glutamine or a functional analogue thereof that retains the characteristics of glutamine in the preparation of an agent for treating atrophy of small intestinal mucosa, the atrophy caused by catabolic dysfunction, **wherein administration of a therapeutically effective amount of the glutamine or analogue thereof is enteral** and **wherein the therapeutically effective amount is greater than or equal to 0.4 grams per kg of body weight per day.** " (emphasis added).

VI. The appellant argued in its grounds of appeal that the conclusions of the Opposition Division were ill founded with respect to the inventive step assessment, mainly

because, in its opinion, as document (E1) did not demonstrate the ability of glutamine to treat mucosal atrophy, there was no reasonable expectation of success and the Opposition Division's analysis was based on a hindsight view, so that the subject-matter of the patent in suit was not obvious.

The appellant filed no further written submissions.

At the beginning of the oral proceedings, the appellant requested a decision on the basis of the facts as they stood on file.

VII. Respondent 2 filed no submission during the appeal proceedings.

None of the respondents attended the oral proceedings.

Respondents 1 and 4 filed written submissions in reply to the appellant's grounds of appeal. They maintained the objections raised before the Opposition Division, with the exception of the ground under Article 52(4) EPC.

As to the appellant's written arguments with respect to inventive step, they held in substance that the claimed second medical application according to the patent in suit was obvious in the light of the prior art, as for instance in the light of document (E1), which suggested the use of exogenous glutamine for treating villus atrophy.

VIII. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the

basis of the main request or, alternatively, on the basis of auxiliary requests 1 to 5, all filed with letter dated 28 May 2002.

Respondents 1 and 4 requested in writing that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. The Board agrees with the positive findings of the Opposition Division as to the objections under Article 123(2) EPC in respect to sufficiency of disclosure and novelty (Opposition Division's decision, pages 4 to 10).

Moreover, having regard to the Board's conclusions in the assessment of inventive step (see below, points 3 and 4) and the fact that the respondents did not adduce any new decisive arguments in these respects, there would appear to be no need to develop these aspects further.

3. *Main request*

Inventive step

3.1 The subject-matter of the contested patent relates to the use of glutamine in the preparation of an agent for treating atrophy of small intestine mucosa caused by catabolic dysfunction (page 4, lines 3 to 5; page 5, lines 45 to 47).

The Board considers that document (51), which concerns the use of glutamine for the preparation of an agent (a total parenteral nutrition (TPN) solution, page 1, right hand column, second table) for treating catabolic dysfunction, namely for maintaining a positive nitrogen balance (page 2, left hand column, paragraphs 2 and 4), represents the closest state of the art.

As acknowledged by the appellant himself, this document discloses a treatment wherein glutamine is administered in a dosage resulting in 0.35 g per kg of body weight per day (appellant's letter dated 28 May 2002, page 9, second paragraph).

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 (51) can be seen in the provision of a further medical use for glutamine.

3.3 This problem is solved by the subject-matter of claim 1, ie by the use of glutamine in the preparation of an agent for treating **atrophy of small intestine mucosa** caused by catabolic dysfunction.

In the light of the working example of the description of the contested patent, the Board has no doubt that the problem has been plausibly solved.

3.4 Thus the question to be answered is whether the proposed solution, ie the treatment of atrophy of small intestine mucosa, would have been obvious to the skilled person in the light of the prior art.

In that respect, document (E1), which concerns a study on the nutritional requirements of the gut in patients fed with intravenously administered nutrients, clearly suggests that the provision of exogenous glutamine to the gut might anticipate abnormalities and maintain mucosal integrity (summary, page 21, right hand column, lines 12 to 24 and lines 25 to 29).

In that context, this document further refers to a study which demonstrates that a reduced level of glutamine produced *inter alia* **villous atrophy** (page 21, right hand column, lines 29 to 35).

It moreover points out that glutamine is not a constituent of TPN solution (page 21, left hand column, lines 46 to 48).

Accordingly, the Board is satisfied that the skilled person faced with the problem as defined above under 3.3 would be prompted to verify whether the glutamine enriched TPN according to document (51) confirms the prediction expressed in document (E1).

3.5 The Board does not agree with the appellant's contention, as part of its main argument, that the claimed indication is inventive because document (E1) is merely a suggestion for further investigations and because it fails to suggest that glutamine is useful in treating atrophy of intestinal mucosa.

It is indeed true that document (E1) suggests further investigations and that the treatment of atrophy intestinal mucosa is mentioned in relation to a different study.

Under the present circumstances, however the Board is convinced that as the agent containing TPN was available on the market and since document (E1) suggests the need for such an glutamine enriched agent for supporting the metabolic demands for the gastrointestinal tract in the case of catabolic dysfunction ("catabolic depleted patient", page 21, right hand column, lines 12 to 24), the skilled person would inevitably check whether the glutamine enriched TPN that he is using for catabolic dysfunction also provides the other promising effect on the gastrointestinal tract suggested in document (E1).

It is also not correct that the inventive step analysis is based on a hindsight view since, as is apparent from the above paragraph, document (E1) mentions *expressis verbis* that the TPN solutions available on the market do not contain glutamine, so that the combination between documents (51) and (E1) is obvious.

In addition, the Board does not accept the appellant's argument that the study referred to in document (E1) is not relevant because the shortage of glutamine in this study was not provoked by catabolism dysfunctions caused by a bacterial glutaminase which could in itself have affected the observed result.

In fact the study referred to in document (E1) establishes a clear relation between the glutamine shortage and the mucosal alteration, whereas it remains silent on any other possible negative effects of the glutaminase on the intestinal mucosa. The Board therefore remains convinced that the skilled person

reading document (E1) had a serious incentive to check whether the addition of exogenous glutamine had a positive effect on the intestinal mucosa.

Finally, whereas the Board agrees with the general argument that one cannot predict whether the administration of a substance will be therapeutic in a subject with an illness that is characterised by a shortage of that substance, this is not however enough to substantiate an inventive step in the present case, since, on the one hand, the prior art suggests the contrary for the specific medical indication of the patent in suit, and, on the other, there is already an available agent on the market (51), so that the skilled person merely needs to verify the ideas expressed in (E1).

Therefore the Board considers that the skilled person would in any case have arrived at the novel medical indication in an obvious way.

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 also no need to consider the remaining claims of the main request.

As claim 1 of the first auxiliary request is identical to claim 1 of the main request, these conclusions hold good for this set of claims as well.

4. *Auxiliary requests 1 to 5*

First auxiliary request

Compared to the main request, claim 1 of this request is restricted to parenteral administration.

The appellant argued that parenteral diets normally did not contain glutamine at the priority date of the patent in suit because of an existing concern with regard to the instability of glutamine and the toxicity of its degradation to toxic compounds.

In that respect, the Board observes that the claims are not restricted to glutamine, but that they encompass "functional analogue thereof".

Accordingly, having regard to document (D9) (page 2, lines 15 to 19, claim 1), which describes the use of a functional analogue of glutamine in intravenous feeding, the Board concludes that auxiliary request 1 also lacks an inventive step.

Second auxiliary request

Compared to the main request, this request has been restricted to a therapeutically effective amount greater than or equal to 0.1 g per kg of body weight per day.

The Board notes that an amount of 0.35 g per kg of body weight per day is already used in the prior art according to document (51) (see point 3.1 above).

Accordingly, as this restriction does not add any distinguishing feature over the prior art, the conclusions under 3.6 hold good for this request as well.

Third auxiliary request

Compared to the main request, this request has been restricted to intravenous feeding as parenteral feeding.

The comments and conclusions made against auxiliary request 1 apply equally to this request as document (D9) concerns intravenous feeding as well.

Fourth auxiliary request

Claim 1 of this request is identical to claim 1 of the second auxiliary request.

The conclusions of the second auxiliary request are therefore the same for this request.

Fifth auxiliary request

Compared to the main request, this request has been mainly restricted to a therapeutically effective amount greater than or equal to 0.4 g per kg of body weight per day.

The Board notes that a similar amount is already used in the prior art according to document (51) (ie 0,35 g) (see above point 3.1).

As no argument has been presented as to why an amount of 0.4 g instead of 0.35 g should involve an inventive step, the conclusions under 3.6 hold good for these requests as well.

Accordingly, the subject-matter of claim 1 of auxiliary request 5 does not fulfil the requirement of inventive step either.

5. *Priority*

As the patent has to be revoked because its subject-matter lacks an inventive step vis-à-vis the prior art documents published before the priority date, the question whether the priority is valid for this subject-matter has no relevance for the decision.

Under these circumstances, there is no need to deal with this point.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar The Chairman

M. Townend U. Oswald