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D E C I S I O N
of 4 March 2003

Case Number: T 0223/01 - 3.3.2

Application Number: 86309899.2

Publication Number: 0249667

IPC: A61K 33/00

Language of the proceedings: EN

Title of invention:
Fluid therapy with L-lactate and/or pyruvate anions

Patentee:
BTG INTERNATIONAL LIMITED

Opponent:
Fresenius AG

Headword:
Fluid therapy/BTG INTERNATIONAL LIMITED

Relevant legal provisions:
EPC Art. 123(2), 54(3)(4)

Keyword:
"Main and first auxiliary requests - no - generalisation not supported"
"Second auxiliary request - novelty - no: exclusion not sufficient to delimit over the prior art disclosure"
"Third auxiliary request - novelty - yes: second medical uses of the claimed compositions not anticipated"

Decisions cited:
-

Catchword:
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Case Number: T 0223/01 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 4 March 2003

Respondent: (Opponent)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 5 December 2000 concerning maintenance of European patent No. 0 249 667 in amended form.**

Composition of the Board:

Chairman: G. F. E. Rampold
Members: J. Riolo
S. U. Hoffmann

Summary of Facts and Submissions

I. European Patent No. 0 249 667 based on application No. 86 309 899.2 was granted on the basis of a set of 5 product claims for Contracting States BE, CH, DE, FR, GB, IT, LI, LU, NL and SE and a set of 5 method claims derived from the product claims for Contracting States AT, GR and ES.

Independent claims 1, 2 and 3 as granted read as follows:

1. A fluid composition for treatment of metabolic acidosis in a living human comprising water having dissolved therein the following components in the respective amounts indicated:

Component	Quantity
Cations	(in mM)
Na^+	0-2400
K^+	0-60
Ca^{++}	0-4
Mg^{++}	0-3
Anions	
l-lactate	0-2400
pyruvate	0-55
d-betahydroxy-butyrate	0-2400
acetoacetate	0-2400

provided that the total amount of l-lactate, pyruvate, d-betahydroxybutyrate and/or acetoacetate anions present in any given solution ranges from 0.1 to 2400 mM with the total amount of said cations being such as to achieve electrical neutrality in such given solution, and further provided that said solution has a pH ranging from 5 to 8.2.

2. A solution for rehydration, electrolyte replacement, and nutrition comprising water having dissolved therein the following components in the respective quantities indicated:

Component	Quantity
Cations	(in mM)
Na^+	130-160
K^+	2-10
Ca^{++}	0,5-2,5
Mg^{++}	0-1,5
Anions	
Cl^-	0-115
l-lactate$^-$	0-55
pyruvate	0-55
d-betahydroxy-butyrate	0-55
acetoacetate	0-55

provided that in any given said solution, the total amount of l-lactate, pyruvate, d-betahydroxybutyrate and/or acetoacetate anions present ranges from 0.1 to 55 mM with the total amount of said cations being such us to achieve electrical neutrality in any given said solution, and further provided that said solution has a pH ranging from 6.0 to 7.5.

3. A solution for dialysis therapy comprising water having dissolved therein the following components in the respective amounts indicated:

Component	Quantity
Cations	(in mM)
Na^+	130-145
K^+	0-4
Ca^{++}	0,5-2,0
Mg^{++}	0-1,0
Anions	
Cl^-	90-120
l-lactate$^-$	0-55
pyruvate	0-55

d-betahydroxy-
butyrate 0-55
acetoacetate 0-55
provided that the total amount of l-lactate, pyruvate, d-betahydroxybutyrate and/or acetoacetate anions present in any given solution ranges from 0.1 to 55 mM with the total number of indicated cations present being such as to achieve electrical neutrality, and also provided that said solution has a pH ranging from 5 to 8.2.

II. Notice of opposition was filed against the granted patent by the respondent (opponent).

The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step.

The following documents were *inter alia* cited during the proceedings:

(E6) English translation of the Japanese document Shimizu Pharmaceutical Co, L-lactate formulation, SOLITA® "Shimizu", pages 1 to 9, February 1983

(E7) WO-A-8600227

III. The interlocutory decision of the Opposition Division established that the patent could be maintained in an amended form under Article 106(3) EPC on the basis of the text of the third auxiliary request.

It rejected the main, first and second auxiliary requests because the amendments introduced in the claims lacked clarity.

As to the third auxiliary request, the Opposition Division expressed the view that it did not contravene the requirements of Article 123(2) and (3) and of Article 84 EPC.

Concerning novelty, the Opposition Division considered that this request was novel and noted that its novelty was, in fact, not contested.

As regards inventive step, the Opposition Division was of the opinion that the only difference over the closest prior art document (E6) was that, contrary to this document which disclosed a Hartmann solution, ie SOLITA®, for the correction of postoperative metabolic acidosis, the patent in suit used this solution for cardiac reperfusion.

Accordingly, it defined the problem to be solved as the provision of a solution for cardiac reperfusion.

Since, in the light of the available prior art, it was not obvious to envisage this particular use for the solution described in document (E6), the Opposition Division considered that the subject-matter of this request involved an inventive step.

It did not follow the opponent's argument that it was clear from the prior art referred to in the patent in suit itself that such a pyruvate solution would be of interest for cardiac reperfusion because this teaching was in fact made in relation to patients suffering from particular heart conditions who were specifically excluded from the scope of uses mentioned in document (E6).

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

V. Oral proceedings were held before the Board on 4 March 2003.

During the oral proceedings, auxiliary requests 2 to 5 were submitted by the appellant. The set of claims of the main and first auxiliary requests were filed on 8 August 2002.

Claims 1 to 5 of the main request correspond to claims 1 to 5 of the granted patent respectively but are reworded in the "second medical use" format and with the amendments that all claims specify that the anions l-lactate and pyruvate are both present in zero amounts and that d-betahydroxybutyrate and acetoacetate anions are not present as a near-equilibrium couple in a milliequivalent ratio of from 6:1 to 0.5:1.

Claims 1 to 5 of the first auxiliary request correspond to claims 1 to 5 of the main request respectively with the amendment that the acetoacetate is present in zero amount, d-betahydroxybutyrate in an amount of 0.1-2400 mM and without the proviso that d-betahydroxybutyrate and acetoacetate anions are not present as a near-equilibrium couple in a milliequivalent ratio of from 6:1 to 0.5:1.

The set of claims of the second auxiliary request corresponds to the set of claims of the main request wherein the use for the treatment of diabetic ketoacidosis is disclaimed from the subject-matter of claim 1.

The set of claims of the third auxiliary request corresponds to the set of claims of the first auxiliary request wherein diabetic ketoacidosis is disclaimed from the subject-matter of claim 1.

The set of claims of the fourth auxiliary request corresponds to the set of claims of the main request without claim 1 and wherein the remaining claims have been renumbered accordingly.

The set of claims of the fifth auxiliary request corresponds to the set of claims of the first auxiliary request without claim 1 and wherein the remaining claims have been renumbered accordingly.

VI. The respondent contested the admissibility of auxiliary requests 2 to 5 filed during the oral proceedings as being late filed.

As to the set of claims of the main request and of the first auxiliary request it considered that the generalisation to the treatment of metabolic acidosis in claim 1 contravened the requirements of Article 123(2) EPC.

It was also of the opinion that the exclusion of the milliequivalent ratio d-betahydroxybutyrate to acetoacetate anions of from 6:1 to 0.5:1 in claim 1 of the main, second and fourth auxiliary requests contravened Article 123(2) because, according to the disclosure in the application as originally filed, this range was disclosed as the preferred range.

It raised an objection under Article 84 EPC to all requests with respect to the amendment that the anions l-lactate and pyruvate (ie, main request, second auxiliary request and fourth auxiliary request) or l-lactate, pyruvate and acetoacetate (ie first auxiliary request, third auxiliary request and fifth auxiliary request) were present in zero amounts.

Finally, it submitted that none of the available sets of claims was novel over the interfering international patent application (E7) under Article 54(3) and (4) EPC in combination with Article 158(2) and (3) EPC.

It indeed argued that the main request, the second auxiliary request and the fourth auxiliary request were anticipated by the disclosure in document (E7) because the exclusion in the claims of the milliequivalent ratio d-betahydroxybutyrate to acetoacetate anions of from 6:1 to 0.5:1 was not sufficient to establish novelty.

The remaining requests were also not novel because, in its view, the prior art compositions described in document (E7) which contained a mixture of d-betahydroxybutyrate and acetoacetate anticipated the claimed composition containing solely d-betahydroxybutyrate.

The respondent did not object with respect to inventive step.

VII. As to the late filing of auxiliary requests 2 to 5, the appellant submitted that the subject-matter of these requests was already announced in its letter dated 4 February 2003 as an answer to the respondent's new objection under Article 123(2) EPC raised in its last letter.

It argued that the generalisation to metabolic acidosis in claim 1 of the main of the first auxiliary requests should be allowable because the statement in the patent in suit that the claimed compositions were not suitable in diabetic ketoacidosis was not proven.

It was also of the opinion that the exclusion of the milliequivalent ratio d-betahydroxybutyrate to acetoacetate anions of from 6:1 to 0.5:1 in claim 1 of the main, second and fourth auxiliary requests did not contravene Article 123(2) EPC. In fact, in its view, this exclusion merely amounted to a restriction of the claimed subject-matter and the fact that this range was disclosed as the preferred range in the application as originally filed supported the proposed restriction but was otherwise irrelevant as far as Article 123(2) EPC was concerned.

Concerning the objection of lack of clarity with respect to the meaning of the amendment which required that the anions l-lactate and pyruvate (ie main request, second auxiliary request and fourth auxiliary request) or l-lactate, pyruvate and acetoacetate (ie first auxiliary request, third auxiliary request and fifth auxiliary request) were present in zero amounts, it considered that it was in fact clear that the only possible meaning was that these anions were not present at all in the claimed compositions and that this clarification was necessary to avoid contravention of Article 123(2) EPC.

As regards novelty, it was of the opinion that the exclusion in the claims of the milliequivalent ratio d-betahydroxybutyrate to acetoacetate anions of from 6:1 to 0.5:1 was sufficient to establish the novelty of the main request, the second auxiliary request and the fourth auxiliary request compared with document (E7) because this document specified that it was not recommended to work outside this range when practising the invention.

As to the remaining requests, it contested the respondent's view that the prior art compositions described in document (E7) which contained a mixture of

d-betahydroxybutyrate and acetoacetate were an anticipation of the claimed composition containing solely d-betahydroxybutyrate.

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 the first auxiliary request both filed on 8 August 2002, or on the basis of the second to fifth auxiliary requests, all filed on 4 March 2003.

The respondent requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. *Admissibility of auxiliary requests 2 to 5*

The Board observes that the subject-matter of auxiliary requests 2 and 3 (ie the exclusion in claim 1 of both requests of diabetic ketoacidosis) was already announced in the appellant's letter dated 4 February 2003 as an answer to the respondent's new objection under Article 123(2) raised in its last letter.

The Board notes also that auxiliary requests 4 and 5 correspond to auxiliary requests 2 and 4 respectively wherein claim 1 has been deleted.

Accordingly, as the respondent could not be surprised by these amendments, the Board decides to admit these requests to the proceedings.

3. *Main request and first auxiliary request*

Article 123(2) EPC

According to the application as originally filed, "Type A solutions of Table II [ie solutions containing d-betahydroxybutyrate and acetoacetate]... are suitable for use in the treatment of certain forms of metabolic acidosis." (page 14, lines 3 to 6).

On page 7, lines 15 and 16, it is moreover specified that "clearly use of d-betahydroxybutyrate or acetoacetate would not be suitable for use in diabetic ketoacidosis".

In that respect, in the absence of any further elements, the Board cannot take into account the appellant's statement made during oral proceedings that it was in fact not proven that d-betahydroxybutyrate or acetoacetate would indeed not be suitable for use in diabetic Ketoacidosis. Therefore, the disclosure in the application as originally filed has to be taken at its face value.

Accordingly, the generalisation to the treatment of metabolic acidosis in claim 1 of the main and first auxiliary requests, which concerns the use of a fluid containing d-betahydroxybutyrate and acetoacetate, infringes the requirements of Article 123(2) EPC.

4. *Second auxiliary request*

4.1 Article 123(2) and (3) EPC

The only objection raised by the respondent under this Article concerns the exclusion in the claims of the milliequivalent ratio d-betahydroxybutyrate to acetoacetate anions of from 6:1 to 0.5:1.

In that respect, the Board notes that this range is disclosed in the application as originally filed on page 9, lines 17 to 22. Accordingly, a clear basis is provided for the excluded range.

The fact that this range is disclosed as a preferred range in the application as originally filed does not change in any way the fact that the introduction of this amendment in the claims has as the sole effect of restricting the subject-matter of these claims.

Accordingly, the Board considers that the requirements of Article 123(2) and (3) are fulfilled.

4.2 Article 84

Concerning the only objection of lack of clarity raised by the respondent with respect to the meaning of the amendment which required that the anions l-lactate and pyruvate be present in zero amounts, the Board considers that the only possible meaning of this amendment is that none of these two anions is present in the claimed compositions.

As the respondent could not provide any other interpretation, the Board concludes that the claimed subject-matter fulfils the requirements of Article 84 EPC.

4.3 Novelty

4.3.1 Document (E7) has been cited under Article 54(3)and (4) EPC as prejudicial to the novelty of the subject-matter of the patent in suit.

As agreed by both parties in their written submissions and during oral proceedings, the compositions disclosed on pages 49 and 50, Table III of document (E7), are the

same as the ones claimed in claim 3 of the second auxiliary request of the contested patent. Moreover, these compositions are also used in dialysis therapy (page 46, lines 7 to 10).

The only point raised by both parties in their written submission and during oral proceedings with respect to novelty is whether the exclusion in the claims of the milliequivalent ratio d-betahydroxybutyrate to acetoacetate anions of from 6:1 to 0.5:1 is sufficient to establish novelty over the compositions disclosed in Table III of document (E7).

In that respect, the Board observes that the milliequivalent ratio d-betahydroxybutyrate to acetoacetate anions disclosed in Table III for the compositions is of **about** 6:1 to 0.5:1.

Accordingly, in the present case, the meaning of the term **about** appears to be of outmost importance for the assessment of novelty.

When looking for its meaning in the particular circumstances of the disclosure of document (E7), the skilled person finds on page 41, lines 20 to 27, the following indication: "Those skilled in the art will realize that in any given solution of this invention one can incorporate an excess of one or more individual members of any one mixture couple of this invention so that (a) the ratio of one member to the other of any given couple and (b) the total quantity of both mixtures or members lies outside of the ranges herein above described [ie about 6:1 to 0.5:1]".

Accordingly, the exclusion of the precise ratio range 6:1 to 0.5:1 in claim 3 is not sufficient to provide for novelty over the compositions disclosed in Table III of document (E7) since compositions outside said range are also encompassed by this disclosure.

In conclusion, the subject-matter of claim 3 of the main request lacks novelty under Article 54(3) and (4) EPC.

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

4.3.2 The appellant argued that the statement on page 41 of document (E7) was devoid of precise technical content and that the document recommended moreover not working outside the preferred range when practising the invention according to (E7) (page 41, lines 29 and 30).

The Board does not dispute the fact that the disclosure in (E7) is not a precise one and that working outside the preferred range is not recommended.

The Board does not however accept that these considerations can provide for novelty for the following reasons:

It is not a requirement for novelty that a novelty-destroying subject-matter be precisely defined. In fact, the only requirement for a subject-matter to be considered as novelty-destroying is that it falls within the scope of what is being claimed. This is the present case.

As to the fact that document (E7) does not recommend working outside the preferred range, the Board notes that the reasons given for that in the document are merely that the efficacy is no better outside the

preferred range (page 41, line 29 to page 42, line 5). Accordingly, there is nothing in (E7) to prevent the skilled person from considering compositions outside the preferred range as belonging to the disclosure of document (E7).

5. *Third auxiliary request*

5.1 Article 123(2) and (3) EPC

No objection under Article 123(2) and (3) EPC was raised with respect to this set of claims and the Board sees no reason to differ.

5.2 Article 84 EPC

Concerning the only objection of lack of clarity raised by the respondent with respect to the meaning of the amendment which required that the anions l-lactate, pyruvate and acetoacetate are present in zero amounts, the Board considers that the only possible meaning of this amendment is that none of these three anions is present in the claimed compositions.

As the respondent could not provide any other interpretation, the Board concludes that the claimed subject-matter fulfils the requirements of Article 84 EPC.

5.3 Novelty

The claimed second medical uses according to claims 1 to 3 are now distinguished from the prior art (E7)in that, contrary to the closest compositions disclosed in document (E7), wherein the couple

d-betahydroxybutyrate/acetoacetate represent a mandatory feature for their medical indications, acetoacetate is absent in the compositions of the claims.

In view of the above, the Board concludes that the subject-matter of claims 1, 2 and 3 of the third auxiliary request fulfils the novelty requirements in Article 54 EPC.

Accordingly, the subject-matter of dependent claims 4 and 5 is also novel.

The Board agrees with the respondent's argument that the disclosure of a mixture of d-betahydroxybutyrate/acetoacetate would anticipate a claim directed to the d-betahydroxybutyrate.

This is not however the present situation since claims 1 to 3 are not product claims claiming d-betahydroxybutyrate *per se*. Claims 1 to 3 are use claims directed to the uses of various complex compositions containing, among others, d-betahydroxybutyrate for the preparation of medicaments for treating various medical indications. Accordingly, only the prior art disclosure of a composition for the same indications falling within the scope of such claims would destroy their novelty.

As the present claims require acetoacetate to be absent from the compositions used, the claimed subject-matter is distinguished from the prior art according to (E7).

5.4 Inventive step

No inventive step objection was raised by the appellant opponent in its grounds of appeal. Moreover, during the oral proceedings, it confirmed that it had no objection to the patent in suit as regards inventive step.

As the Board sees no reason to differ, inventive step is not at issue.

Accordingly, there is no need to consider the further requests.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of the appellant's third auxiliary request filed on 4 March 2003 (claims 1 to 5) and for the description to be adapted thereto.

The Registrar: The Chairman:

A. Townend G. Rampold