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Datasheet for the decision of 28 November 2008

Case Number: T 1009/06 - 3.3.02

Application Number: 93902846.0

Publication Number: 0629133

IPC: A61K 51/00

Language of the proceedings: EN

Title of invention:
Peptide-metal ion pharmaceutical applications

Patentee:
Rhomed, Incorporated

Opponent:
ANTISOMA PLC
Schering AG

Headword:
Peptide-metal ion pharmaceutical applications/RHOMED, INC.

Relevant legal provisions:
EPC Art. 123(2)

Relevant legal provisions (EPC 1973):
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Keyword:
"Main request - admissibility (no): reformatio in peius"
"Auxiliary request - Article 123(2) (no): subject-matter of claim 1 not specifically disclosed in the original application"

Decisions cited:
G 0009/92

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1009/06 **-** 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 28 November 2008

Party as of right:
(Opponent 1)

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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 25 April 2006 concerning maintenance of European patent No. 0629133 in amended form.**

Composition of the Board:

Chairman: J. Riolo
Members: A. Lindner
J. Van Moer

Summary of Facts and Submissions

I. European patent No. 0 629 133 based on application No. 93 902 846.0 was granted on the basis of a set of 36 claims.

Independent claim 1 reads as follows:

"1. A method of preparing a pharmaceutical composition containing a labelled peptide suitable for administration to a patient, characterised by:
(a) obtaining or preparing a peptide substrate comprising a biological function domain (BD) and a medically useful labelling metal ion binding domain (MD), said substrate having a formula selected from:
$(R_1)-[Y_1]_n-(R_2)$,
$(R_1)-[Y_1-(R_2)-Y_1]_n-(R_3)$ and
$(R_1)-[Y_1-(R_2)-Y_2]_n-(R_3)$
where
R_1, R_2 and R_3 each comprise an amino acid sequence containing from 0 to 20 amino acids, Y_1 and Y_2 are amino acids containing S N and/or 0 capable of complexing with ions of a transition metal selected from Zn, Cu, Sn, Co and Ni, and
n is an integer from 1 to 6
wherein
said MD is selected from $[Y_1]_n$, $[Y_1-(R_2)-Y_1]_n$ and $[Y_1-(R_2)-Y_2]_n$ and
said BD comprises at least one of R_1, R_2 and R_3 and includes an amino acid sequence containing from 1 to 20 amino acids.
(b) reacting said substrate in a pharmaceutically acceptable aqueous buffer solution with a source of ions of a said transition metal so as to form complexes

of said S, N and/or 0-containing amino acid and said transition metal ions, and

(c) reacting said complexed substrate in said buffer solution with a medically useful labelling metal ion, said labelling ion having a higher order of binding than said transition metal ion so as to replace the transition metal ion by said labelling metal ion on said MD, thereby producing said composition comprising a labelled peptide in said buffer,

provided that where said substrate includes disulfide bonds these are first reduced by incubation of the substrate with a reducing agent and excess reducing agent is afterwards removed."

II. Two oppositions were filed against the granted patent. The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step, under Article 100(b) EPC for insufficient disclosure of the invention and under Article 100(c) EPC because its subject-matter extended beyond the content of the application as filed.

III. In the decision pronounced on 3 November 2005, the opposition division maintained the patent in amended form on the basis of auxiliary request 1 filed at the oral proceedings. The main request was rejected for lack of novelty. As regards the claims of the auxiliary request, the opposition division came to the conclusion that the subject-matter claimed therein met the requirements of Articles 54, 56, 83, 84 and 123(2) EPC. In connection with the requirements of Article 123(2) EPC, it was held that that the wording "amino acid comprising at least one element selected from the group

consisting of sulfur, nitrogen or oxygen, which is available or can be made available for binding…" included amino acids comprising all three elements.

IV. The appellant (opponent 2) lodged an appeal against that decision.

V. The parties were invited to oral proceedings by an official communication dated 4 August 2008. The opponent 1 declared by letter dated 8 September 2008 that he would not attend the oral proceedings.

VI. The respondent-patentee declared by letter dated 22 October 2008 that he would not attend the oral proceedings.

VII. Oral proceedings before the board were held on 28 November 2008. Claim 1 of the auxiliary request reads as follows:

"1. A method of preparing a pharmaceutical composition containing a labeled peptide suitable for administration to a patient, characterized by:
(a) obtaining or preparing a peptide substrate comprising a biological function domain (BD) and a medically useful labeling metal ion binding domain (MD), said substrate having a formula selected from:
$(R_1)-[Y_1]_n-(R_2)$,
$(R_1)-[Y_1-(R_2)-Y_1]_n-(R_3)$ and
$(R_1)-[Y_1-(R_2)-Y_2]_n-(R_3)$
where
R_1, R_2 and R_3 each comprise an amino acid sequence containing from 0 to 20 amino acids, Y_1 and Y_2 are amino acids containing S N and/or 0 capable of complexing

with ions of a transition metal selected from Zn, Cu, Sn, Co and Ni, and
n is an integer from 1 to 6
wherein
said MD is selected from $[Y_1]_n[Y_1-(R_2)-Y_1]_n$ and $[Y_1-(R_2)-Y_2]_n$ and
said BD comprises at least one of R_1, R_2 and R_3 and includes an amino acid sequence containing from 1 to 20 amino acids.

(b) reacting said substrate in a pharmaceutically acceptable aqueous buffer solution with a source of ions of a said transition metal so as to form complexes of said S, N and/or 0-containing amino acid and said transition metal ions, and

(c) reacting said complexed substrate in said buffer solution with a medically useful labeling metal ion, said labeling ion having a higher order of binding than said transition metal ion so as to replace the transition metal ion by said labeling metal ion on said MD, thereby producing said composition comprising a labeled peptide in said buffer,

provided that where said substrate includes disulfide bonds these are first reduced by incubation of the substrate with a reducing agent and excess reducing agent is afterwards removed; with the proviso that the peptide substrate is not GRGDGGC; maGGGRGDF; $YRALVDTLKFVTQAEGAKC\cdot NH_2$; $mmpGGGRALVDTLK\cdot NH_2$; $PenGGGRALVDTLK\cdot NH_2$ or $maGGGGRALVDTLK\cdot NH_2$, wherein ma = mercaptoacetic acid, Pen = L-penicillamine and mmp = 2-mercapto-2-methylpropionic acid; with the proviso that the metal ion binding domain is not of the formula

Cp(aa)Cp, wherein Cp is a protected cysteine and (aa) is an amino acid and wherein the metal ion binding domain is covalently bound to the biological function domain."

VIII. The appellant's arguments, as far as they are relevant for this decision, can be summarised as follows:

As far as the definitions of Y_1 and Y_2 in claim 1 are concerned, the appellant held that amino acids containing e.g. S + O or S + N + O were not specifically disclosed in the original application, neither by explicit nor by implicit disclosure. As a consequence, the requirements of Article 123(2) EPC were not met.

IX. As far as they are relevant for this decision, the respondent-patentee's arguments in his written submissions can be summarised as follows:

In connection with the definition of Y_1 and Y_2 in claim 1 it was argued that the original application disclosed amino acids containing at least one element selected from the group containing S, N and O, which disclosed amino acids comprising two or even all three elements. Moreover, all amino acids comprised O and N in their basic peptidic structure. Thus, the original application cited cysteine, cystine, penicillamine and deacylated methionine as suitable amino acids, each of which comprised S, N and O. As a consequence, the definition of Y_1 and Y_2 in claim 1 was in accordance with the requirements of Article 123(2) EPC.

X. The appellant (opponent 2) requested that the decision under appeal be set aside and that the European patent be revoked.

The respondent (patentee) requested in writing that the patent be maintained on the basis of the claims as granted or, alternatively on the basis of the claims upheld by the opposition division.

Reasons for the Decision

1. The appeal is admissible.

2. Main request:

In the present case, opponent 2 is the sole appellant. In the decision under appeal the patent was maintained in amended form on the basis of the auxiliary request. According to decision G 9/92 (OJ EPO 1994, 875-891), the patentee, by not filing an appeal, has indicated that he has no intention to contest the maintenance of the patent in the version accepted by the opposition division (see point 16 in Reasons for the Decision). In the present case, the return to the claims as granted cannot be reconciled with the principle of avoiding a ***reformatio in peius***. As a consequence, the main request is not admissible.

3. Auxiliary request:

3.1. Claim 1 - Article 123(2) EPC:

In present claim 1, the rests Y_1 and Y_2 are defined as amino acids containing S, N and/or O capable of complexing with ions of a transition metal selected from Zn, Cu, Sn, Co and Ni. By linking the three elements with **and**/or [emphasis by the board], amino acids comprising S + N + O capable of complexing with ions of a transition metal are specifically disclosed as representatives for the rests Y_1 and Y_2.

The original application defines the rests Y_1 and Y_2 as amino acids comprising at least one element selected from the group consisting of S, N or O which is available… (see claims 3 and 7 of the original application). This definition specifically discloses amino acids comprising only S as defined above, amino acids comprising only N as defined above and amino acids comprising only O as defined above; furthermore it conceptually includes but does not specifically disclose amino acids comprising S + N, S + O, N + O and S + N + O. In order to be allowable under Article 123(2) EPC, it is not sufficient that a specific combination of elements is conceptually included in the scope provided by a disclosure in the original application, but it is necessary that it is specifically disclosed or individualised. As this is not the case for the combination S + N + O, the subject-matter of claim 1 of the auxiliary request does not meet the requirements of Article 123(2) EPC.

3.2. Further arguments of the respondent-patentee:

It was held that all amino acids comprise N and O in their basic peptidic structure. This is not contested by the board, but in this context the question arises whether each N or O present in the amino acid molecule is capable of complexing with ions of a transition metal selected from Zn, Cu, Sn, Co and Ni as required by the wording of claim 1. If yes, then any sulfur-containing amino acid would provide a basis for amino acids containing S + N + O, as the latter two elements would be mandatorily present and therefore be implicitly disclosed. However, it has to be taken into consideration that the functional feature "capable of complexing with ions of a transition metal selected from Zn, Cu, Sn, Co and Ni" has a limiting character. This is confirmed by the disclosure on page 13, lines 38-42 of the original application, where it is indicated that the N-containing amino acids comprise histidine, lysine and arginine and the terminal amino group of peptides. Likewise, the O-containing amino acids include aspartic acid, glutamic acid, tyrosine and the terminal carboxy group of peptides (see page 13, lines 42-44). This passage clearly shows that neither the nitrogen of the α-amino group nor the oxygen of the α-carboxyl group forming the peptide bonds is capable of complexing with ions of a transition metal selected from Zn, Cu, Sn, Co and Ni, unless they are in a terminal position. Amino acids which are not in a terminal position require an additional N- and O-containing functional group as well as a S-containing functional group in order to represent an amino acid containing S + N + O as defined in present claim 1. As a consequence, this argument cannot succeed.

3.3. In view of this finding, an evaluation of the further objections raised under Article 123(2) EPC as well as of the grounds of opposition raised under Article 100(a) and 100(b) EPC is not necessary.

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 J. Riolo