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D E C I S I O N
of 27 May 2004

Case Number: T 0497/02 - 3.3.4

Application Number: 93203087.7

Publication Number: 0587255

IPC: C07K 7/10

Language of the proceedings: EN

Title of invention:
Insulinotropic hormone

Applicant:
THE GENERAL HOSPITAL CORPORATION

Opponent:
-

Headword:
Insulinotropic hormone/GENERAL HOSPITAL

Relevant legal provisions:
EPC Art. 83
RPBA Art. 10
Guidelines for Examination in the EPO, 2001
C.IV.4.7; C.IV.4.12

Keyword:
"Sufficiency of disclosure (no)"

Decisions cited:
T 0222/00

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0497/02 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 27 May 2004

Appellant: THE GENERAL HOSPITAL CORPORATION
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Boston, MA 02110 (US)

Representative: Thomas, Philip John Duval
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 20 November 2001 refusing European application No. 93203087.7 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairwoman: U. Kinkeldey
Members: M. Wieser
S. C. Perryman

Summary of Facts and Submissions

I. The appeal was lodged by the Applicants (Appellants) against the decision of the Examining Division to refuse under Article 97(1) EPC the patent application EP 93 203 087.7, publication number EP 0 587 255 having the title: "Insulinotropic hormone". The application is a divisional application of the earlier application with the publication number EP 0 305 387 in accordance with Article 76 EPC.

II. Appellant's request (Annex C to the decision under appeal) in relation to which the Examining Division decided the substantive issues consisted of claims 1 and 2 which read:

"1. The use of a peptide having insulinotropic activity substantially similar to GLP-1 (7-37) in the preparation of an agent for the treatment of diabetes mellitus, wherein the peptide consists of the GLP-1(7-37) sequence:

His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Gly

but where the sequence lacks one amino acid.

2. The use as claimed in claim 1, wherein the peptide has the formula:

$$(1)\ H^2N - X - CO - R^1$$

wherein R^1 represents OH, OM, or NR^2R^3;
where M is a pharmaceutically acceptable cation or a C_1-C_6 branched or unbranched alkyl group;
each of R^2 and R^3 are the same or different and independently represent a hydrogen atom or a C_1-C_6 branched or unbranched alkyl group; and
X is a peptide according to claim 1;
or an acid salt thereof."

III. The Examining Division decided at oral proceedings not to allow into the proceedings under Rule 86(3) EPC two requests filed by the Appellants on 21 September 2001, as they both contained a claim 3 which was not based on the application as filed, contrary to the requirements of Article 123(2) EPC. Claim 3 read:

"3. The use as claimed in claim 1 or claim 2, wherein the agent is for the treatment of maturity onset diabetes mellitus."

IV. It view of this refusal the Applicants agreed to continue at the oral proceedings before the Examining Division on the basis of a previous request consisting of claims 1 and 2 shown in section (II) above.

The Examining Division decided that the application did not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, contrary to the requirements of Article 83 EPC. The technical effect expressed in the claims, namely the usefulness of a peptide consisting of, or comprising the sequence of amino acids 7 to 37 of glucagon-like peptide I (GLP-1(7-37)) lacking one amino acid, for the preparation of an agent for the

treatment of diabetes mellitus, had not been disclosed in the application.

Moreover, the decision under appeal contains a remark on page 3, saying that the Examining Division "...is also of the opinion that the involvement of an inventive step cannot be recognised...".

V. The Appellants had requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of one of the requests identified in the Grounds of Appeal filed on 19 March 2002.

VI. The Board expressed its preliminary opinion in a communication dated 28 October 2003, which was annexed to the summons to attend oral proceedings on 27 May 2004.

VII. On 26 March 2004 the Appellants filed a new main request and five auxiliary requests on which a patent should be granted. The requests read as follows:

Main request:

"1. Use of a peptide in the preparation of an agent for the treatment of diabetes mellitus, wherein the peptide either
(i) consists of the GLP-1(7-37) sequence:

His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Gly; or

(ii) or a functional derivative of the GLP-1 (7-37) peptide which has insulinotropic activity substantially similar to GLP-1 (7-37) and consists of the GLP-1 (7-37) sequence set out above but where the sequence lacks one amino acid.

2. Use of a peptide having insulinotropic activity substantially similar to GLP-1 (7-37) in the preparation of an agent for the treatment of diabetes mellitus, wherein the peptide has the formula:

(1) H^2N - X - CO - R^1

wherein R^1 represents OH, OM, or NR^2R^3;
where M is a pharmaceutically acceptable cation or a C_1-C_6 branched or unbranched alkyl group;
each of R^2 and R^3 are the same or different and independently represent a hydrogen atom or a C_1-C_6 branched or unbranched alkyl group; and
X consists either of the GLP-1 (7-37) sequence: His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Gly; or a functional derivative of GLP-1 (7-37) sequence set out above where the sequence lacks one amino acid; or an acid addition salt thereof.

3. Use as claimed in claim 1 or claim 2, wherein the agent is for the treatment of maturity onset diabetes mellitus."

First auxiliary request:

"1. Use of a peptide having insulinotropic activity substantially similar to GLP-1 (7-37) in the

preparation of an agent for the treatment of diabetes mellitus, wherein the peptide consists of the GLP-1(7-37) sequence:

His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Gly

but where that sequence lacks one amino acid.

2. Use of a peptide having insulinotropic activity substantially similar to GLP-1 (7-37) in the preparation of an agent for the treatment of diabetes mellitus, wherein the peptide has the formula:

(1) H^2N - X - CO - R^1

wherein R^1 represents OH, OM, or NR^2R^3;
where M is a pharmaceutically acceptable cation or a C_1-C_6 branched or unbranched alkyl group;
each of R^2 and R^3 are the same or different and independently represent a hydrogen atom or a C_1-C_6 branched or unbranched alkyl group; and
X consists either of the GLP-1 (7-37) sequence: His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Gly but where the sequence lacks one amino acid or an acid addition salt thereof."

Claim 3 was identical to claim 3 of the main request.

Second auxiliary request:

Claims 1 and 3 were identical to claims 1 and 3 of the first auxiliary request.

"2. Use of a peptide having insulinotropic activity substantially similar to GLP-1 (7-37) in the preparation of an agent for the treatment of diabetes mellitus, wherein the peptide has the formula:

(1) H^2N - X - CO - R^1

wherein R^1 represents NR^2R^3;
where R^2 and R^3 are the same and represent a hydrogen atom and X is a peptide according to claim 1; or an acid addition salt thereof."

Third auxiliary request:

"Consists of the claims of the Main, first or second auxiliary requests amended to delete the wording "substantially similar to GLP-1(7-37)" in Claims 1 or 2."

Fourth auxiliary request:

"Consists of the Claims of the Main, first, second or third auxiliary requests with Claim 3 deleted."

Fifth auxiliary request:

"Consists of the claims of the Main, first, second, third or fourth auxiliary requests with Claim 1 or 2 deleted."

VIII. The following comments were provided by the Appellants on pages 3 to 4 of their letter with regard to these requests:

"You will see that the third auxiliary request consists of the simple deletion of a phrase from the earlier requests. Also, the fourth and fifth auxiliary request consist of the simple deletion of a claim.

We believe that the above presentation of the third to fifth auxiliary requests is clear and is the best way of avoiding a proliferation of auxiliary requests. However, if the Board would prefer us to file separate sets of claims for each of the auxiliary requests, we would be happy to do so. Unless the Board contacts us to the contrary, we assume that it is happy with our presentation of auxiliary requests.

If the Board considers that there is any other patentable subject-matter, we request that we be allowed to submit a further auxiliary request to that subject-matter."

IX. Two days before the scheduled date the Board were informed that the Appellants would not attend oral proceedings.

X. Oral proceedings were held on 27 May 2004 in the absence of the Appellants pursuant to Rule 71(2) EPC.

XI. The submissions of the Appellants, as far as they are relevant for the present decision, may be summarised as follows:

The statement in the appealed decision relating to lack of inventive step should be disregarded by the Board, as it was added by the Examining Division after the oral proceedings. The refusal to allow into the proceedings the Appellant's requests of 21 September 2001 at the oral proceedings under Rule 86(3) EPC amounted to a procedural violation. Appellant's right to be heard had been violated (Article 113(1) EPC), because the Examining Division did not send a communication first, giving the reasons for refusing the requests pursuant to the then applicable Guidelines for Examination in the EPO, part C, chapter VI, point 4.12.

The requirements of Article 83 EPC were met by the present application. There were only 31 possible members in the group of GLP-1(7-37) peptides lacking one amino acid and the application taught on pages 6 and 7 how to produce them. No undue experimentation would have been required to assay the insulinotropic properties of these 31 peptides, as the relevant assay methods were disclosed in the present application. Moreover, testing the 31 compounds involved, for determining their effectiveness in treating diabetes, by using methods well known in the art, would not represent undue burden.

Several post published documents have confirmed that GLP-1(7-36) had the same biological effects and the same activity as GLP-1(7-37).

It would be most unfair for the Board to refuse the application on the basis that no supporting evidence had been filed, as there had been no clear indication in the earlier proceedings that in the absence of such evidence a negative decision might be taken. Such procedure would violate Appellant's right to be heard according to Article 113(1) EPC.

Reasons for the Decision

Procedural matter

1. The appeal meets the requirements of Articles 106 to 108 EPC and Rule 64 EPC and is thus admissible.

2. For the purpose of these appeal proceedings, the Appellant's complaint in connection with the refusal of the Examining Division to allow into the proceedings the claim requests filed on 21 September 2001, only becomes relevant in accordance with Article 10 of the Rules of Procedure of the Boards of Appeal (RPBA) if fundamental deficiencies are apparent in the first instance proceedings which require that the Board should remit the case to the first instance without considering the substantive issues. Such a fundamental deficiency would be a procedural violation of such gravity that it vitiates the basis on which Examination Division made its decision, making it necessary for the first instance to decide anew after a properly conducted procedure.

3. Two matters require consideration as to whether they amount to such a fundamental deficiency, firstly the exercise of the Examining Division of its discretion under Rule 86(3) EPC, and secondly the Appellant being informed of the reasons for the exercise of this discretion only at the oral proceedings before the Examining Division and not earlier or in writing.

4. That the new dependent claim 3 sought to be introduced into the proceedings by these belated requests was considered not to be in conformity with Article 123(2) EPC is considered by the Board an adequate and reasonable justification for the Examining Division to exercise its discretion under Rule 86(3) EPC not to allow these new claim requests into the proceedings. The Board can see no procedural violation arising from the refusal itself, let alone any fundamental deficiency.

5. The Appellant, relying on the then applicable Guidelines for Examination in the European Patent Office Part C Chapter VI point 4.12, has complained that he was sent no written communication prior to the oral proceedings giving the reasons for the refusal under Rule 86(3) EPC, nor any prior telephone indication, and that this amounted to a violation of his rights under Article 113(1) EPC. The then applicable point 4.12 read:

'If a request for amendment is to be refused under Rule 86(3), the applicant must first in compliance with Art. 113(1) be sent a communication giving the reasons for refusing the amendment. In the case of a situation as described in VI, 4.10 the applicant should be

invited at the same time to request grant of the patent on the basis of the preceding acceptable version of the documents. If the applicant maintains his request for the amendment, the application must be refused under Article 97(1) since, in these circumstances, there is no text of the application which has been agreed by the applicant and allowed by the Examining Division (Article 113(2)).'

6. This has to be read in the context of the purpose of Rule 86(3) EPC, which was to give the Examination Division a discretion to refuse amendments to the claims not made in answer to the first communication, so as to ensure that the examination procedure is brought to a conclusion in as few actions as possible (Cf. then applicable Guidelines Part C Chapter VI point 4.7). From this and the text of point 4.12, the Board sees the purpose of the then applicable Guidelines as being to give an applicant an opportunity to avoid the situation of having a negative decision merely on the ground of there being no text agreed to by the applicant. Point 4.12 is not seen as applicable to a situation where oral proceedings take place, as the requirements of Article 113(1) EPC can then be met, as was done in the present case, by the applicant being informed of the objection at the oral proceedings and being afforded the opportunity to revert to a request submitted earlier which had been allowed into the proceedings.

7. Article 113(1) EPC merely requires applicants to be afforded the opportunity to present their comments on the grounds on which the European Patent Office bases its decision: the Article does not require a written

communication nor does it specify how much time applicants should be afforded to consider and present their comments. An applicant cannot expect to amend his claim request(s) a bare month before the date set for oral proceedings, and still before the oral proceedings be sent a written communication or given a telephone notification indicating that the Examining Division proposes to exercise its discretion under Rule 86(3) EPC against the admission of the new request(s), and the reasons for this. The applicant must expect to have to deal with any problems with such late requests at the oral proceedings.

8. In conclusion, the Board sees no procedural violations as having occurred in this case, and no need or basis for remitting the case to the Examining Division pursuant to Article 10 RPBA.

9. The Board will confine itself to considering whether the reason for refusal under Article 83 EPC by the Examination Division of the request before it was correct, and also applies to the requests now pending before the Board. The Board sees other issues under Rule 86(3) EPC, and Articles 84 and 123(2) EPC, but since the Appellants instructed their representatives not to be present at the oral proceedings before the Board they have not been raised or commented on by the appellants, and cannot form a basis for the Board's decision.

10. The Board sees the reason for refusal and core objection of insufficiency by the Examining Division as being in that the claimed subject matter of use of a peptide corresponding to the amino acid sequence of

GLP-1(7-37) lacking one amino acid for the preparation of an agent for a treatment of diabetes mellitus is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, contrary to the requirements of Article 83 EPC, because on the information in the application plus common general knowledge the skilled person would not know which, if any at all, of the thirty odd peptides would fulfil this function. It would thus be undue burden, contrary to the requirement of sufficiently clear and complete disclosure, for a skilled person to research the claimed area for himself to find out if anything worked.

11. Independent claims 1 and 2 of the new main request now put forward cover this same subject matter, as well as additional subject matter namely the use of the full GLP-1(7-37) peptide itself, which is described as functional in the application as filed and which was not objected to by the Examining Division as it was not part of the subject matter of the claims before the first instance. However the Board does not see that broadening the subject matter of a claim to also cover a specific use that is sufficiently described, avoids the objection of insufficiency as to the remaining subject matter of the claim if this objection is valid as to this remaining subject matter by itself. Nor does the slightly modified wording compared to the claims considered by the Examining Division do anything to avoid the core objection on insufficiency in relation to the independent claims 1 and 2 of the main request.

12. Claims 1 and 2 of each of the first and second auxiliary requests are directed only to use of a

peptide corresponding to the amino acid sequence of GLP-1(7-37) lacking one amino acid for the preparation of a treatment of diabetes mellitus, and again the Board considers that the slight verbal differences compared to the claims considered by the Examining Division contribute nothing to avoiding the core objection of insufficiency.

13. While the Board considers the way of presenting the various further auxiliary requests to be quite unacceptable, it appears clear that each auxiliary request will still contain at least one claim open the same core objection of insufficiency on the basis of which the first instance refused the application.

14. Thus if the Board considers the core objection of insufficiency to apply, none of the requests now put forward is allowable.

15. On page 3, lines 10 to 23, in the summary of the invention, the application discloses that GLP-1(7-37), "the insulinotropic hormone", is useful in the study of the pathogenesis of maturity onset diabetes mellitus and in the therapy for this disease. Page 4, lines 37 to 41 states that the invention pertains to polypeptides which are functionally similar to GLP-1(7-37), but whose sequence may contain or lack one or more amino acids compared to the naturally occurring sequence.

16. Neither the description nor the specific examples 1 to 7 disclose that a peptide falling under the definition of 'GLP-1(7-37) lacking one amino acid' has been tested

for its ability to be used for the preparation of an agent for the treatment of diabetes mellitus.

Appellants line of argumentation, namely that the invention is sufficiently disclosed because a skilled person can produce the 31 peptides falling under this definition and test them for the claimed effect is not conclusive. What is undue burden must be decided on a case by case basis.

17. The patent application does not contain any evidence that even a single one of these 31 peptides in fact shows the required biological activity. The skilled person, when trying to carry out the claimed invention, has to isolate, synthesize or produce by recombinant DNA technology said 31 peptides, and to perform tests and assays to determine whether they possess the required biological activity. This considerable research program imposed on the skilled person has to be performed with no certainty of even a single success. That any amino acid can be omitted seems impossible, so that the expectation must be that most, if not all of the minus-one GLP-1(7-37) peptides will not work.

18. The Board would like to emphasize that the biological activity of proteins is highly dependent on their secondary and tertiary structures, resulting from their primary structure, their amino acid sequence. It is common general knowledge that the deletion of a single amino acid may have great influence on the three-dimensional folding of peptides or parts thereof. There is no basis in the application to conclude that any of the 31 peptides involved, or, if any, how many thereof will show secondary and tertiary structures, giving

them properties that make them candidates for use in the treatment of diabetes mellitus. In this situation, the Board can only conclude that the invention is insufficiently disclosed.

19. The Appellants further argued that several post published documents have confirmed that the activity of GLP-1(7-36) is the same as that of GLP-1(7-37).

If a disclosure is insufficient in that it provides no guidance for performing the invention, a reference to later documents showing how such performance was accomplished at a later date is incapable of curing the insufficiency (cf T 222/00 15 January 2003).

20. It is up to the Appellants to file evidence in support of their case. The decision under appeal, which decided that the present application does not meet the requirements of Article 83 EPC, was dispatched in November 2001. The Board considers that the Appellants have had ample time to provide evidence supporting their line of argumentation. Therefore, the Board does not agree with the Appellants, that it would be unfair to refuse the application without giving them an opportunity to file further evidence.

21. The Board comes to the decision that the present patent application does not disclose the claimed invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, contrary to the requirements of Article 83 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona U. Kinkeldey