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Datasheet for the decision of 29 November 2019

Case Number: T 1250/16 - 3.3.04

Application Number: 09715588.1

Publication Number: 2252324

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Language of the proceedings: EN

Title of invention:
Alkaline phosphatase for increasing the activity of the immune system of a mammal at risk of inflammatory diseases

Patent Proprietor:
Alloksys Life Science B.V.

Opponent:
AM-Pharma B.V.

Headword:
Alkaline phosphatase/ALLOKSYS LIFE SCIENCE

Relevant legal provisions:
EPC Art. 100(c), 123(2)
RPBA Art. 13

Keyword:
Main request - added subject-matter (yes)
Late filed auxiliary request - admitted into proceedings (no)

Decisions cited:

Catchword:
-

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Case Number: T 1250/16 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 29 November 2019

Appellant: (Opponent)	AM-Pharma B.V. Rumpsterweg 6 3981 AK Bunnik (NL)
Representative:	Dörries, Hans Ulrich df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte PartG mbB Theatinerstrasse 16 80333 München (DE)
Respondent: (Patent Proprietor)	Alloksys Life Science B.V. Gildenbring 74 3981 JG Bunnik (NL)
Representative:	van Kooij, Adriaan Arnold & Siedsma Bezuidenhoutseweg 57 2594 AC The Hague (NL)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 14 March 2016 rejecting the opposition filed against European patent No. 2252324 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairwoman	R. Morawetz
Members:	B. Claes
	L. Bühler

Summary of Facts and Submissions

I. The opponent (appellant) filed an appeal against the decision of the opposition division rejecting the opposition to European patent No. 2 252 324 with the title "*Alkaline phosphatase for increasing the activity of the immune system of a mammal at risk of inflammatory diseases*". The patent derives from European patent application No. 09 715 588.1, which was filed as an international application under the PCT with the number PCT/EP2009/001603 ("application as filed" or "application") and published as WO 2009/106368.

Claims 1, 2, 4 and 6 of the application as filed read:

"1. Use of an ectophosphatase for the preparation of a medicament for the prophylaxis of a mammal at risk of inflammatory diseases.

2. Use according to claim 1, wherein said ectophosphatase is selected from the group consisting of alkaline phosphatase, nucleotidases (CD39, CD73), and apyrase (CD39 like ATP/ADPase).

4. Use according to any of the claims 1 to 3, wherein said prophylaxis comprises induction of endogenous ectophosphatase levels.

6. Use according to any of the claims 1 to 5, wherein said condition is selected from the group consisting of surgery, digestive tract diseases, respiratory diseases, skin diseases, burn wounds, smoke inhalation, intoxication, severe blood loss, food poisoning,

chemotherapy, radiation therapy, severe trauma liver diseases, and immuno compromised conditions."

II. The patent was opposed under Article 100(a) EPC, on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), and under Articles 100(b) and 100(c) EPC.

The sole claim of the patent as granted read:

"1. Alkaline phosphatase for use in the prophylaxis of patients undergoing surgery, said patients being at risk of inflammatory diseases resulting from surgery, by induction of endogenous alkaline phosphatase, said prophylaxis comprises intravenous administering of a therapeutically effective amount of alkaline phosphatase to said patients undergoing surgery."

III. In the statement of the grounds of appeal the appellant submitted, *inter alia*, that the claim as granted related to added subject-matter (Article 100(c) EPC).

IV. After the patent proprietor (respondent) had replied to the appeal, the appellant made further submissions.

V. The parties were summoned to oral proceedings and the board subsequently issued a communication with its preliminary assessment of the appeal. The board indicated that it was inclined to agree with the appellant that, for the reasons they had submitted, claim 1 as granted related to added subject-matter and that it was of the preliminary opinion that, *inter alia*, the patent did not sufficiently disclose the claimed invention (Article 100(b) EPC).

VI. In reply to the board's communication the respondent filed three auxiliary requests and further arguments to the effect that claim 1 as granted did not relate to added subject-matter.

The sole claim of auxiliary request 3 read (amendments made compared with claim 1 of the main request are highlighted):

"1. Alkaline phosphatase for use in the prophylaxis of patients undergoing surgery, said patients being at risk of inflammatory diseases resulting from surgery, by induction of endogenous liver type tissue non-specific alkaline phosphatase, said prophylaxis comprises intravenous administering a bolus of a therapeutically effective amount of alkaline phosphatase followed by intravenous infusion of the alkaline phosphatase to said patients undergoing surgery."

VII. In response, the appellant requested that the newly filed auxiliary requests not be admitted into the appeal proceedings and submitted arguments in support of this request.

VIII. During the oral proceedings the respondent withdrew auxiliary requests 1 and 2. At the end of the oral proceedings the chair announced the board's decision.

IX. The appellant's arguments, in so far as they are relevant for the decision on added subject-matter, can be summarised as follows:

Main request (patent as granted) - claim 1

A combination of the features relating to "*intravenous administering*" of AP and "*induction of endogenous alkaline phosphatase*" as specified in the claim was disclosed in the application as filed solely as a particular embodiment of the invention, namely in an embodiment wherein a bolus of bovine AP, followed by a 36-hour intravenous infusion of 5.6 IU/kg/hour, was administered to human patients,resulting in a peak plasma level of endogenous tissue non-specific AP; see page 5, lines 17 to 21; page 8, lines 5 to 14, and example 1 of the application as filed. Hence, intravenous administration of bovine AP such that endogenous AP was induced in humans was disclosed solely in the context of, and as inextricably linked to, a particular treatment protocol, i.e. bolus administration followed by a 36-hour intravenous infusion of 5.6 IU/kg/hour.

The claim was not limited to the particular treatment protocol disclosed, or to bovine AP. Indeed, it related to any form of intravenous administration of any type of AP, for which there was no basis in the application as filed. The reference in claim 1 to intravenous administration of AP without the limitation that it was administered in accordance with a specific treatment regime thus constituted an intermediate generalisation of specific embodiments present in the application as filed, without there being any basis for such a generalisation.

The passage starting on page 5, line 22, of the description had to be read in the context of the preceding passage and related to the same embodiment as page 5, lines 17 to 21.

The passage starting on page 5, line 30, of the description and the passages on page 6 did not specify that administration was intravenous and it was also not directly and unambiguously derivable from the application as filed as a whole that administration should be carried out intravenously; see e.g. page 10, last paragraph.

Claim 4 as filed related to the induction of endogenous ectophosphatase levels in general but not to the induction of endogenous AP levels as claimed (emphasis in original). Claim 2 as filed only referred to AP as the ectophosphatase to be administered. Claim 4 in combination with claim 2 as filed therefore did not disclose the specific combination of the administration of AP and the induction of endogenous AP as claimed.

X. The respondent's arguments, in so far as they are relevant for the decision on added subject-matter, can be summarised as follows:

Main request (patent as granted) - claim 1

Although the application as filed did not contain an explicit disclosure of the claimed combination of features, the treatment protocol referred to on page 5, lines 17 to 21, of the description was not the sole disclosure in the application as filed of a treatment protocol that led to the induction of endogenous AP.

The passage in fact had to be read in the context of the passages preceding and following it. Those passages related to administrations of AP which were not limited to bolus administration and did not limit the induction of endogenous AP levels to a particular treatment

protocol. Hence, the skilled person reading the passage on page 5, lines 17 to 21, in its context would understand that *any* intravenous administration of AP would result in increased plasma levels of endogenous phosphatase.

Claim 4 as filed specified that the prophylactic use of an ectophosphatase according to claims 1 to 3 involved the induction of endogenous ectophosphatase levels and claim 2 specified that this ectophosphatase was AP. The induction of endogenous ectophosphatase levels was therefore disclosed in claim 4 as filed as not inextricably linked to any dosage regime or treatment protocol.

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

The respondent (patent proprietor) requested that the appeal be dismissed (main request) or, alternatively, that the patent be maintained in amended form on the basis of the claim of auxiliary request 3 filed by letter dated 24 October 2019.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is therefore admissible.

Main request (patent as granted) - claim 1

Amendments (Article 100(c) EPC)

2. The opposition division held that the subject-matter of claim 1 as granted had a basis in claim 6 in combination with claims 1 and 4 and the teaching on page 5, lines 17 to 21, of the application as filed.

3. The appellant reiterated that the claim as granted related to added subject-matter (Article 100(c) EPC) because the application as filed did not disclose the combination of the features relating to "*intravenous administering*" of AP and "*induction of endogenous alkaline phosphatase*" as claimed (see section IX).

4. While the respondent concurred with the appellant to the extent that the application as filed failed to explicitly disclose the claimed combination of features, it submitted that the treatment protocol in the passage on page 5, lines 17 to 21, of the description was not the sole treatment protocol disclosed in the application as filed that led to the induction of endogenous AP. In fact, this passage had to be read in the context of the passages preceding and following it which related to administrations of AP which were not limited to bolus administration and did not limit the induction of endogenous AP levels to a particular treatment protocol.

5. More specifically, the passages referred to by the respondent as forming the context in which the passage on page 5, lines 17 to 21, had to be read were:

on page 5, lines 10 to 16:

"*The present invention demonstrates that supplemental alkaline phosphatase in patients undergoing surgery not only such anti-inflammatory responses are observed, but also an induction is evoked of an endogenous secondary alkaline phosphatase that is inhibited by L-HA (L-homo arginin), known to act as an inhibitor of tissue non specific AP.*";

on page 5, lines 22 to 25:

"*Surprisingly however, the endogenous AP that emerges is an AP with the kinetic profile having an observed overall plasma residence time in the order of about 20-22 hours.*";

on page 5, line 30 to page 6, line 2:

"*Hence, where administration of AP during acute inflammation is reported to combat local or systemic endotoxin- and other phosphate-containing substrates-induced inflammation, AP prophylaxis improves the defense against a new inflammatory insult by triggering the release of sustainable alkaline phosphates in the circulation.*"; and

on page 6, lines 3 to 21:

"*The surprising implication of this provides, amongst others, the following advantages:*

- *AP acts like an acute phase protein, where high levels of physiological active AP have a protective anti-inflammatory effect;*
- *Supplemental pre-surgical plasma levels benefit clinical outcome in acute inflammation;*

- *Patients suffering from or at risk of inflammatory conditions/diseases are protected by pre-treatment or treatment with physiological active AP, which will elevate their endogenous physiological levels*
- *retreatment of AP supplementation during surgery or at time points post surgery will perpetuate the induction the endogenous alkaline phosphatase. The anti inflammatory effects of alkaline phosphatase thus are prolonged."*

6. The board notes, however, that none of these passages discloses intravenous administration of AP. The board is further unable to identify any statement in these passages, or in the rest of the description of the application as filed, that intravenous administration was envisaged to apply generally. On the contrary, on page 10, last paragraph, the application discloses that the administration of phosphatase may be "*intravenous, subcutaneous, intraperitoneal, by inhalation or oral*" and no preference for intravenous administration is evident. Hence, the board concurs with the appellant that the skilled person would not derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing ("gold standard"; see decision G 2/10, OJ EPO 2012, 376), from the passages referred to by the respondent the disclosure that any form of intravenous administration of AP leads to the induction of endogenous AP.

7. The board furthermore concurs with the appellant that intravenous administration of AP inducing endogenous AP in humans is disclosed in the application as filed solely in the context of, and as inextricably linked to, a particular treatment protocol, i.e. bolus administration of bovine AP followed by a 36-hour intravenous infusion of 5.6 IU/kg/hour resulting in a

peak plasma level of endogenous tissue non-specific AP (see page 5, lines 17 to 21, for the passage in the description of the application as filed, and example 1 and the paragraph on page 8, lines 5 to 14, for the legend of the corresponding Figure 1).

8. The reference in claim 1 to intravenous administration of AP in the absence of the limitation that it is to be administered as a bolus of bovine AP followed by a particular regime of intravenous infusion therefore constitutes an intermediate generalisation of the specific embodiment disclosed on page 5, lines 17 to 21, of the application as filed, which presents the skilled person with new technical information for which the application provides no basis.

9. The respondent further argued that claim 4 of the application as filed specified that the prophylactic use of an ectophosphatase according to any of claims 1 to 3 led to the induction of endogenous ectophosphatase levels independently of a dosage regime or treatment protocol and that claim 2 specified that this ectophosphatase was AP.

10. In this respect too, however, the board concurs with the appellant and notes that claim 4 as filed refers to the "*induction of endogenous ectophosphatase levels*" and not to the induction of endogenous AP (see section I). Furthermore, dependent claim 2 as filed merely refers to AP as the ectophosphatase to be used for the prophylaxis and not to AP as the ectophosphatase that is induced (see section I). Therefore, the combination of claims 2 and 4 as filed provides no basis for the induction of endogenous AP and the respondent's argument (see point 9) fails for this reason alone.

11. Accordingly, in view of the above considerations, the board decides that the granted claim relates to added subject-matter (Article 100(c) EPC).

Auxiliary request 3 - admission into the proceedings (Article 13(1) RPBA)

12. According to Article 13(1) RPBA, any amendment to a party's case after it has filed its grounds of appeal or reply to the grounds of appeal may be admitted and considered only at the board's discretion. This discretion is to be exercised in view of, *inter alia*, the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy. Furthermore, Article 13(3) RPBA additionally stipulates that amendments sought to be made after oral proceedings have been arranged are not to be admitted if they raise issues the board or the other party cannot reasonably be expected to deal with without adjournment of the oral proceedings.

13. In the case in hand, the claim request was not filed by the respondent with its reply to the appeal (see sections IV and VI), but only after the parties had been summoned to oral proceedings and the board had issued a communication in which it expressed its preliminary opinion on substantive issues raised by the appeal, including, *inter alia*, that claim 1 of the patent as granted was considered to relate to added subject-matter (see section V). The admission of the request is therefore governed by Article 13(1) and (3) RPBA.

14. The respondent justified filing the request at this late stage of the proceedings on account of the fact that, although the opponent, in the opposition

proceedings, had raised a multitude of objections under Article 123(2) EPC, some of them filed as late as during the oral proceedings, the opposition division had held that the main request satisfied the requirements of Article 123(2) EPC and the board's negative opinion on this issue in the communication had been the first indication that there might be a problem with claim 1 of the patent as granted.

15. In the board's view, the fact that the board's preliminary opinion went against the decision of the opposition division is, in itself, not a persuasive reason for the respondent's failure to file appropriate fall-back positions with its reply to the appeal of the opponent. Indeed, the board notes in this context that the assessment presented by the board in its communication did not introduce any new issue in the context of added subject-matter as compared with the appellant's submissions in the statement of grounds of appeal. The board simply followed an argument made by one of the parties to the proceedings and referred explicitly to this argument in its communication. If a party to the proceedings were allowed to amend its case in view of a preliminary opinion by the board in which the board agrees with the position expressed by the adverse party in its statement of grounds of appeal or reply thereto, the aim of Articles 12 and 13 RPBA would be seriously undermined.

16. The respondent further submitted that the auxiliary request did not raise *prima facie* new problems and constituted a *bona fide* attempt to overcome the deficiencies in claim 1 of the main request. Filing fall-back positions with its reply to the appeal so as to take into account each and every one of the multitude of objections would have required the

drafting and submission of a large number of (possibly permutated) auxiliary requests. Filing the auxiliary request after the board had issued its preliminary opinion allowed the respondent to more efficiently focus the drafting on and limit it to the contentious issues.

17. However, the board notes that claim 1 of auxiliary request 3 is not merely the result of the combination of the subject-matter of an independent claim with that of a claim depending on it, but involves a combination of changing the wording of the claim and the addition of two particular features allegedly disclosed in the description as filed.

18. As a result, the claim, in addition and as submitted by the appellant, raises *prima facie* new added subject-matter issues under Article 123(2) EPC as well as clarity issues under Article 84 EPC. Indeed, it was, *inter alia*, questionable whether the application disclosed that it was actually the endogenous liver type AP that was induced (see page 5, lines 25 to 27, and page 23, lines 10 to 12, of the application as filed). Furthermore, it was questionable whether the meaning of the terms "liver type tissue non-specific" and "bolus" was clear. Therefore, admitting the auxiliary request would have raised questions which the board deemed to be inappropriately complex at that stage of the proceedings.

19. In view of these considerations, the board, in the exercise of its discretion under Article 13(1) and (3) RPBA, decided not to admit auxiliary request 3 into the appeal proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

I. Aperribay R. Morawetz

Decision electronically authenticated