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Datasheet for the decision of 12 November 2019

Case Number: T 0860/16 - 3.3.04

Application Number: 09730293.9

Publication Number: 2265285

IPC: A61K39/35, A61K39/36

Language of the proceedings: EN

Title of invention:
Mucosomal allergen-specific immunotherapy with initial dosing after start of pollen season

Patent Proprietor:
ALK-Abelló A/S

Opponents:
Merck Patent GmbH
Leeming, John Gerard
Stallergenes

Headword:
Sublingual immunotherapy/ALK-ABELLÓ

Relevant legal provisions:
EPC Art. 54, 56

Keyword:
Main (sole) request - inventive step (no)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 0860/16 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 12 November 2019

Appellant I: (Opponent 1)	Merck Patent GmbH Frankfurter Strasse 250 64293 Darmstadt (DE)
Appellant II: (Opponent 3)	Stallergenes 6, rue Alexis de Tocqueville 92160 Antony Cedex (FR)
Representative:	Lavoix 2, place d'Estienne d'Orves 75441 Paris Cedex 09 (FR)
Respondent: (Patent Proprietor)	ALK-Abelló A/S Bøge Allé 6-8 2970 Hørsholm (DK)
Representative:	Inspicos P/S Kogle Allé 2 2970 Hørsholm (DK)
Party as of right: (Opponent 2)	Leeming, John Gerard J.A. Kemp & Co. 14 South Square Gray's Inn London, Greater London WC1R 5JJ (GB)
Representative:	J A Kemp LLP 14 South Square Gray's Inn London WC1R 5JJ (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 23 February 2016 rejecting the opposition filed against**

European patent No. 2265285 pursuant to Article 101(2) EPC.

Composition of the Board:

Chair	B. Claes
Members:	R. Morawetz
	P. de Heij

Summary of Facts and Submissions

I. The appeals by opponent 1 ("appellant I") and opponent 3 ("appellant II") lie from the opposition division's decision rejecting the oppositions against European patent No. 2 265 285 (the "patent"). The patent is entitled "*Mucosomal allergen-specific immunotherapy with initial dosing after start of pollen season*" and derives from European patent application No. 09 730293.9, which was filed as an international application under the PCT with the number PCT/EP2009/054186 ("application as filed" or "application") and published as WO 2009/124954.

II. The following documents are referred to in this decision:

D3: Calderon M.A. *et al.*, Allergy (2007), vol. 62, pages 958 to 961

D24: D'Anneo R.W. *et al.*, Allergol Immunopathol (March 2008), vol. 36(2), pages 79 to 84

D32: WO2004/047793

D34: Kleine-Tebbe J. *et al.*, Allergy (2006), vol. 61, pages 181 to 184

III. Three oppositions were filed against the patent. The patent was opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC), lack of inventive step (Article 56 EPC), exclusion from patentability (Articles 53 c) and 54(5) EPC), and under Article 100(b) and 100(c) EPC. The opposition division decided, *inter alia*, that the subject-matter of claim 1

as granted was novel over the disclosure of document D24 and that it involved an inventive step regardless of whether the disclosure in document D24 or document D32 was considered to represent the closest prior art.

IV. Prior to filing their statement of grounds of appeal appellant II (Stallergenes S.A.) requested that their status as opponent be transferred to Stallergenes. In support of this request appellant II filed a copy of a "Projet de traité d'apport partiel d'actif entre Stallergenes S.A. (société apporteuse) et Stallergene (société bénéficiaire)" and a copy of an "Extrait Kbis".

V. In their statement of grounds of appeal, appellant I submitted arguments, *inter alia*, to the effect that the subject-matter of claim 1 as granted was not novel over the disclosure of document D24 and lacked an inventive step over the disclosure in document D24 alone or in combination with that of document D34.

VI. In their statement of grounds of appeal, appellant II submitted arguments to the effect that the subject-matter of claim 1 as granted lacked an inventive step over the disclosure of document D32 representing the closest prior art, taken alone or in combination with the disclosure in document D24.

VII. With their reply to the appeals, the patent proprietor (respondent) maintained the set of claims as granted as their main request and filed sets of claims of auxiliary requests 1 to 41.

VIII. Further written submissions were made by the appellants and the respondent.

IX. The board scheduled oral proceedings as requested by the parties, and issued a communication pursuant to Article 15(1) RPBA in which it indicated, *inter alia*, its preliminary opinion on the construction of claim 1 of the main request and on the lack of novelty of the claimed subject-matter over the disclosure of document D24. The board further noted that it considered the transfer of the opponent's party status requested by appellant II to be acceptable.

X. In response, the appellants and the respondent made further written submissions in support of their respective cases.

XI. Oral proceedings before the board took place on 12 November 2019. Opponent 2 was absent, as notified previously in writing. The respondent made auxiliary request 17 its main (sole) request and withdrew all other claim requests.

Claim 1 of the main (sole) request read as follows:

"1. A solid dosage form formulated to be suitable for sublingual administration comprising a seasonal allergen composition for use as a medicament in allergen-specific immunotherapy for preventing or treating allergy to said seasonal allergen composition in a subject by sublingual administration, wherein the solid dosage form is administered in a mono-dose dosage regimen, wherein initial administration is performed within the allergen season of the allergen composition, wherein the dosage regimen does not comprise a separate up-dosing phase and maintenance phase in that the same

treatment dose is administered throughout the treatment period and wherein the allergen composition is an allergen extract."

XII. At the end of the oral proceedings the Chair announced the board's decision.

XIII. Appellant I's arguments, submitted in writing and during the oral proceedings, as far as they are relevant for this decision, are summarised as follows:

Main (sole) request - claim 1

Claim construction

The term "*mono-dose dosage regimen*" was understood by a person skilled in the art to mean a treatment regimen applying a dosage form which always comprised the same amount of allergen (mono-dose) and could comprise an up-dosing phase; see paragraphs [0015], [0016] and [0042] of the patent.

Paragraphs [0064] and [0065] of the patent could not be used to interpret the claim.

The patent defined an "*up-dosing phase*" as a treatment phase in which increasing doses were administered until an effective and safe treatment dose had been reached, which dose was used throughout the maintenance phase.

Novelty (Article 54(2) EPC) - Document D24

Disclosed was co-seasonal sublingual immunotherapy (SLIT) with a solid mono-dose dosage form without an up-dosing phase (page 80, left-hand column, second paragraph and page 81, left-hand column, first

paragraph).

What was called a "*build-up phase*" in document D24 was not an "*up-dosing phase*" as defined in the patent, because after the "*build-up phase*" with 1000 AU tablets the therapy was continued with the same tablets.

The Lais® allergoid tablet (see page 81, left-hand column, first sentence) contained a chemically modified allergen extract from *Parietaria* pollen, which was standardised to have an allergenic activity of 1000 allergenic units (AU). The allergoid was thus not non-allergenic, but just less allergenic or hypo-allergenic.

In Sicily the *Parietaria* allergen was seasonal as there was a pause in August and December (see page 80, left hand column, last paragraph of document D24).

In light of paragraph [0025] of the patent, the allergoid in document D24 fell within the definition of an allergen extract.

The claimed subject-matter therefore lacked novelty over the disclosure in document D24.

Inventive step (Article 56 EPC)

Closest prior art and technical problem to be solved

Document D24 represented the closest prior art and the subject-matter of claim 1 differed from the disclosure in that an allergen *extract* was used. The objective technical problem to be solved was the provision of an alternative composition for use in allergen-specific sublingual immunotherapy.

Obviousness of the claimed solution

Faced with the technical problem the skilled person would consider all known allergen compositions, especially those on the market, such as the GRAZAX® tablet (document D34).

The claim was not limited to any specific amount of allergenic units and the skilled person would not have concerns about the safety of using a composition having a low amount of allergenic units.

Document D34 examined the safety of GRAZAX® for sublingual immunotherapy and concluded that the grass allergen tablet could be administered without any up-dosing schedule in doses from 25 000 to 1 000 000 SQ-T with no severe or serious adverse events (page 183, discussion, first sentence).

Knowing that even a dosage of 1 000 000 SQ-T of potentially more allergenic grass allergens than the allergoid used in document D24 was safe when administered pre-seasonally without up-dosing, the skilled person would not have hesitated to replace the allergoids used in the intraseasonally initiated treatment of document D24 with an allergen extract, at least in a low dose.

The recommendation in document D3 to start eight weeks before the season did not relate to safety concerns but to obtain clinical efficacy.

The claimed subject-matter therefore did not involve an inventive step.

XIV. Appellant II's arguments, submitted in writing and during the oral proceedings, as far as they are relevant for this decision, are summarised as follows:

Main (sole) request

Admittance

The respondent had not provided any substantiation when filing this claim request with their reply to the appeals as auxiliary request 17. The request should be held inadmissible.

Claim 1

Claim construction

The term "*mono-dose dosage regimen*" meant that a composition with a given amount of allergen was used.

The complete definition of a dosage regimen included an indication of the frequency of administration; see also paragraphs [0039], [0064] and [0065] of the patent.

In the "*mono-dose dosage regimen*" the frequency was not defined, meaning that the number of doses administered per day could vary.

Inventive step

Closest prior art and technical problem to be solved

When starting from the disclosure in document D24, the objective technical problem was to provide an alternative composition for use in allergen-specific sublingual immunotherapy.

Obviousness of the claimed solution

Grass pollen allergy was a widespread type of allergy for which sublingual immunotherapy (SLIT) that could be initiated in the season of grass pollination was of great interest.

GRAZAX® (see e.g. document D34) was the only authorised drug consisting of a solid dosage form comprising a seasonal allergen, i.e. a grass pollen extract of *Phleum pratense*.

Document D24 disclosed that a treatment with a seasonal allergen that was safe and effective had been initiated during the season directly with the dose used in the maintenance phase (see abstract).

For solving the objective technical problem, the skilled person had no reason to avoid a known allergen extract which was regularly used in SLIT.

The claimed subject-matter therefore did not involve an inventive step.

XV. The respondent's arguments, submitted in writing and during the oral proceedings, as far as they are relevant for this decision, are summarised as follows:

Main (sole) request - claim 1

Claim construction

A "*mono-dose dosage regimen*" was a dosage regimen in which the patient received the same treatment dose (mono-dose) over the entire treatment period; see

paragraphs [0015] and [0016] of the patent.

The meaning of "*mono-dose dosage regimen*", namely that a fixed dose and a fixed frequency were used, i.e. the same dose was given each day, could be derived from paragraphs [0064] and [0065] of the patent.

The meaning of the terms "*up-dosing phase*" and "*maintenance phase*" was explained in paragraph [0017] of the patent.

Novelty (Article 54(2) EPC) - Document D24

Document D24 did not teach a mono-dose dosage regimen because the dose differed between days 1, 2 and 3. In the regimen disclosed in document D24 an up-dosing took place by three increasing doses being administered over three consecutive days.

The immunised subjects disclosed in document D24 were not allergic to the allergoids. Indeed, page 81, right-hand column, end of first paragraph and page 82, right-hand column, disclosed that no adverse events were observed.

The allergen in document D24 was not a seasonal allergen.

The allergoid in document D24 was a chemically modified product which did not fall within the definition of an allergen extract given in paragraph [0025] of the patent.

Inventive step (Article 56 EPC)

Closest prior art and technical problem to be solved

Document D24 represented the closest prior art and the appellants had correctly formulated the objective technical problem to be solved.

Obviousness of the claimed solution

Document D24 disclosed the administration of an allergoid, i.e. a cross-linked allergen preparation known to be much less prone to provoking hypersensitivity than the natural allergen.

It went against the teaching of document D24 to use GRAZAX®, which was less safe than an allergoid and for which adverse effects had been reported in document D34. Moreover, document D3 taught that administration of GRAZAX® should start eight weeks prior to the grass pollen season.

XVI. Opponent 2 (a party as of right) did not submit any arguments or requests during the appeal proceedings.

XVII. Appellant I and appellant II requested that the decision under appeal be set aside and that the patent be revoked.

XVIII. The respondent requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the set of claims of the main request, filed as auxiliary request 17 with letter dated 17 November 2016.

Reasons for the Decision

1. The appeals comply with Articles 106 to 108 and Rule 99 EPC and are therefore admissible.

Transfer of opponent 3's party status from Stallergenes S.A. to Stallergenes

2. In the course of the appeal proceedings, opponent 3 (appellant II), Stallergenes S.A., requested a transfer of the opponent's party status to Stallergenes (see section IV.).

3. Based on the documentary evidence provided (see section IV.) the board is satisfied that all the assets of the business to which the opposition related have been transferred to Stallergenes (see also decision G 4/88, OJ EPO 1989, 480, Order and Case Law of the Boards of Appeal, 9th edition 2019, section III.O.2.1). This was not disputed by the respondent.

4. Accordingly, the board decides that the requested transfer of the opponent's party status from Stallergenes S.A. to Stallergenes can be allowed, and that Stallergenes is a party to these appeal proceedings (opponent 3/appellant II).

Main (sole) request - claim 1

5. Although admittance of this set of claims was contested by appellant II, there is no need to give reasons for its admittance, since, for the reasons given below, the request could not be allowed.

Claim construction

"*mono-dose dosage regimen*"

6. The claimed solid dosage form comprising a seasonal allergen composition is stipulated as being administered in a "*mono-dose dosage regimen*" (see section XI.).

7. The parties disagree on the interpretation of the term "*mono-dose dosage regimen*". While it is common ground that the term implies that a fixed treatment dose is used, the appellants submit that the term leaves *open* the frequency of administration of that treatment dose, whereas the respondent submits that the term also implies a *fixed* frequency of administration of the treatment dose.

8. It is established jurisprudence of the boards of appeal that the skilled person should try to arrive at an interpretation of the claim which is technically sensible and takes into account the whole disclosure of the patent (see Case Law of the Boards of Appeal of the European Patent Office, 9th edition 2019, II.A.6.1).

9. In the board's judgement the interpretation advanced by the appellants is supported by paragraph [0039] of the patent, pursuant to which "*the dosage regimen used in the present invention may be any conventional dosage regimen used for mucosal allergen-specific immunotherapy in respect of doses, number of doses per day, duration of treatment and frequency of administration*" (see lines 55 to 57). Indeed, it is evident from this paragraph that the definition of a "*dosage regimen*" requires (i) an indication of the dose used and (ii) an indication of the number of doses per

day, duration of treatment and frequency of administration.

10. The respondent relied on Example 1 of the patent to argue that "*mono-dose dosage regimen*" means that a fixed dose and a fixed frequency were used, namely daily administration of the same dose.

11. Example 1 of the patent discloses that "*GRAZAX® was administered to patients once daily*" (see paragraph [0064], lines 8 to 9) while the "*dosage was 75,000 SQ-T*" (see paragraph [0065], line 14).

12. The board notes that Example 1 merely represents a particular embodiment of the dosage regimen of the invention and that the limiting feature - daily administration of the same dose - is absent from the claim. It is established jurisprudence of the boards of appeal that for the purpose of assessing novelty and inventive step, the scope of a claim should not be cut down by implying into it features which appear only in the description (see Case Law of the Boards of Appeal of the European Patent Office, 9th edition 2019, II.A.6.3.4).

13. Therefore, the board concludes that a fixed frequency of administration as disclosed in paragraph [0064] of the patent is not to be considered a limiting feature for the claim.

14. From the above considerations the board concludes that the term "*mono-dose dosage regimen*" implies that only one dose of allergen composition is used, while the frequency of administration is undefined. Accordingly, the term "*mono-dose dosage regimen*" does not imply that the number of doses given is always the same or that

the regimen excludes administration of more than one dose per day.

"*up-dosing phase and maintenance phase*"

15. The claim further stipulates that the dosage regimen does not comprise a separate "*up-dosing phase and maintenance phase*" (see section XI.).

16. The patent provides that "*the term 'up-dosing phase' means a period of treatment during which the doses of allergen composition administered are gradually increased to reach a full dose level, which is used in the following maintenance phase, and the up-dosing phase ends when the said full dose level is reached, i.e. immediately subsequent to the administration of the first full dose*" and that "*the term "maintenance phase" means a period of treatment in continuation of the up-dosing phase and during which a full dose of allergen composition is administered, the maintenance phase starting immediately subsequent to the administration of the first full phase*" (see paragraph [0017], page 4, line 57 to page 5, line 6).

Novelty (Article 54 EPC) - Document D24

17. Document D24 discloses *Parietaria* co-seasonal sublingual immunotherapy (SLIT) in rhinitic and/or asthmatic patients allergic to *Parietaria* with a chemically modified (carbamylated) allergen extract from *Parietaria* pollen (Lais®), which has been standardised to have an allergenic activity of 1000 allergenic units (AU) and prepared as orosoluble tablets of 1000 AU. The disclosed treatment schedule is as follows: during a three-day build-up phase one tablet was given on the first day, two tablets were

given on the second day, three tablets were given on the third day, and subsequently a maintenance dose of one tablet per week was given for the rest of the therapy. No adverse events were observed and the study concluded that at six months the allergoid SLIT showed itself to be effective and safe (see title, abstract and page 81, left hand column, first paragraph).

18. In the board's view the dosage regimen which always uses the same dose of allergen, 1000 AU, falls within the meaning of the term "*mono-dose dosage regimen*" (see point 14. above). Furthermore, what is called the "*build-up phase*" in document D24 is not an "*up-dosing phase*" as defined in the patent (see point 16. above), as the disclosed "*build-up phase*" starts with the full dose of 1000 AU, which is the very same dose as used in the maintenance phase.

19. In the board's view the mere absence of adverse events does not indicate to the skilled person that the subjects were not allergic to the allergoid, as alleged by the respondent. To the contrary, the fact that the allergoid is "*biologically standardised in allergenic units (AU)*" (see page 81, left hand column, first paragraph) indicates to the skilled person that the allergoid is indeed allergenic. The board therefore concurs with appellant I that the allergoid in document D24 is not non-allergenic, but rather less allergenic or hypo-allergenic compared with the non-modified, i.e. natural *Parietaria* allergen.

20. Also, the respondent's further argument that the *Parietaria* allergen of document D24 is not seasonal is not found to be persuasive either, because the document states, on page 80, left-hand column, last paragraph of document D24, that in Sicily - where the study was

performed - there is a pause in pollination in August and in December.

21. However, the board does not concur with appellant I's argument that the skilled person reading paragraph [0025] of the patent would understand that an allergen extract can also include an allergoid. In fact, paragraph [0025] of the patent discloses that "*the allergen composition may be an allergen extract, a purified fraction of an allergen extract, a modified allergen, a recombinant allergen and a mutant of a recombinant allergen*" (see lines 9 to 10) and further that "*the modified allergen may be any allergen derivative modified by e.g. chemical, physical or enzymatic treatment, including e.g. allergoids*" (see lines 13 to 14). Thus, according to paragraph [0025], a modified allergen is not a specific form of an allergen extract but an alternative form of allergen composition. The board therefore concurs with the respondent that the allergoid in document D24 does not fall within the definition of an "*allergen extract*" in claim 1.

22. The board concludes from the above that document D24 discloses a solid dosage form formulated to be suitable for sublingual administration comprising a seasonal allergen composition and its use in allergen-specific immunotherapy according to a dosage regimen that falls within the dosage regimen of claim 1. The sole difference between the disclosure of document D24 and the subject-matter of claim 1 is that in document D24 a chemically modified allergen extract, i.e. an allergoid, is used while according to claim 1 an allergen extract is used.

23. The subject-matter of claim 1 is thus not anticipated by the disclosure of document D24.

Inventive step (Article 56 EPC)

Closest prior art and technical problem to be solved

24. The parties were in agreement that document D24 represented the closest prior art; that the claimed subject-matter differs from this disclosure in that the allergen composition is an allergen *extract* and that the objective technical problem to be solved is the provision of an alternative composition for use in allergen-specific sublingual immunotherapy. The board sees no reason to differ.

Obviousness of the claimed solution

25. The board concurs with the appellants that the skilled person faced with the technical problem would consider all known allergen compositions, especially those on the market, for solving the problem. In fact, unless there are reasons to exclude a particular one, it suffices to choose any of these compositions, which are then all equally obvious solutions.

26. One commercially available allergen composition is GRAZAX®, i.e. grass allergen tablets containing grass allergen extract of standardised quality from *Phleum pratense* which are used in sublingual immunotherapy of grass pollen allergy (see e.g. document D34, page 181, title and right-hand column, third paragraph or document D3, page 958, paragraph bridging left-hand and right-hand columns).

27. However the respondent argued that the skilled person would not consider GRAZAX® because it was less safe than an allergoid as adverse effects had been reported (see document D34) and because document D3 taught that administration of GRAZAX® should start eight weeks prior to the grass pollen season.

28. The board notes that document D34 discloses that "*the grass allergen tablet was tested without any up-dosing schedule in doses from 25 000 to 1 000 000 SQ-T, and it was tolerated with no severe or serious AEs* [adverse events]" (emphasis added, see page 183, right-hand column, third paragraph). The board is thus not persuaded that the adverse events disclosed in document D34 - reportedly neither severe nor serious - would have deterred the skilled person from using GRAZAX® instead of an allergoid. Furthermore, the board concurs with the appellants that the skilled person would simply use a lower dose of the allergen extract if they had any concerns about safety.

29. Document D3 concerns SLIT treatment with GRAZAX® tablets initiated pre-seasonally without up-dosing and continued throughout the entire grass pollen season (see page 958, first paragraph) and discloses that "*pre-seasonal treatment of approximately 8 weeks or more is necessary to obtain clinical efficacy in the grass pollen season*" (emphasis added, see page 960, left-hand column, last paragraph). The board notes that document D3 does not disclose that pre-seasonal treatment is necessary for reasons of safety.

30. Considering that document D24 establishes (see point 17. above) that a treatment which is safe and effective can be initiated with a seasonal allergen during the season directly with the dose used in the

maintenance phase, the board holds that the teaching of document D3 would not deter the skilled person from using GRAZAX® intraseasonally.

31. From the above the board concludes that the skilled person faced with the technical problem would have readily used a GRAZAX® tablet for sublingual immunotherapy of grass pollen allergy in the mono-dose dosage regimen disclosed in document D24 and would thus have arrived at an embodiment of claim 1 in an obvious manner.

32. Therefore, the claimed subject-matter does not meet the requirements of Article 56 EPC.

Conclusion

33. The sole claim request forming part of the appeal proceedings does not meet the requirements of Article 56 EPC. Accordingly, the patent cannot be maintained on the basis of this request and, in the absence of another, allowable claim request, the patent is to be revoked.

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 B. Claes

Decision electronically authenticated