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Datasheet for the decision of 5 February 2019

Case Number: T 1729/15 - 3.3.04

Application Number: 10007477.2

Publication Number: 2263688

IPC: A61K39/095, A61K39/385, A61P31/04, C12P19/04

Language of the proceedings: EN

Title of invention:
Neisseria meningitidis combination vaccines

Patent Proprietor:
GlaxoSmithKline Biologicals SA

Opponent:
Pfizer Inc.

Headword:
Neisseria meningitidis combination vaccines/GLAXOSMITHKLINE

Relevant legal provisions:
EPC Art. 56

Keyword:
Main request, auxiliary request 1 - inventive step (no)

Decisions cited:
G 0009/92, T 0606/89

Catchword:

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 1729/15 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 5 February 2019

Appellant: (Patent Proprietor)	GlaxoSmithKline Biologicals SA Rue de l'Institut 89 1330 Rixensart (BE)
Representative:	Dalton, Marcus Jonathan William GlaxoSmithKline Global Patents (CN925.1) 980 Great West Road Brentford, Middlesex TW8 9GS (GB)
Respondent: (Opponent)	Pfizer Inc. 235 East 42nd Street New York, NY 10017 (US)
Representative:	Pfizer European Patent Department 23-25 avenue du Docteur Lannelongue 75668 Paris Cedex 14 (FR)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 30 June 2015 concerning maintenance of the European Patent No. 2263688 in amended form.**

Composition of the Board:

Chair	G. Alt
Members:	R. Morawetz
	L. Bühler

Summary of Facts and Submissions

I. The appeal of the patent proprietor (appellant) lies against the interlocutory decision of the opposition division that European patent No. 2 263 688 can be maintained in amended form.

II. The patent is entitled "*Neisseria meningitidis combination vaccines*" and was granted in respect of European patent application No. 10 007 477.2, a divisional application of European patent application No. 06 075 175.5, which in turn is a divisional application of European patent application No. 02 755 452.6, filed on 20 June 2002. The patent claims the priority of GB application No. 0 115 176, filed on 20 June 2001.

III. An opposition was filed against the patent. 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), under Article 100(b) and 100(c) EPC.

IV. The opposition division decided that the subject-matter of the main request (claims as granted) did not extend beyond the content of the (earlier) application as filed and that the patent disclosed the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. However, it held that the subject-matter of claims 1, 2, 3, 7 and 10 lacked novelty (Article 54 EPC). The subject-matter of claim 1 of auxiliary request 1 was found to lack an inventive step (Article 56 EPC). The patent was

maintained in amended form on the basis of the set of claims of auxiliary request 2 and an adapted description.

V. With the statement of grounds of appeal the appellant filed a main request and auxiliary requests 1 and 2. These claim requests were the same as the claim requests underlying the decision under appeal.

Claim 1 of the main request and of auxiliary requests 1 and 2 read as follows:

"1. A kit comprising: (a) conjugated capsular oligosaccharide from *N.meningitidis* serogroup A, in lyophilised form; and (b) one or more further antigens in liquid form."

"1. A kit comprising: (a) conjugated capsular oligosaccharide from *N.meningitidis* serogroup A, in lyophilised form, wherein the serogroup A saccharide has an average degree of polymerisation of between 10 and 20; and (b) one or more further antigens in liquid form."

"1. A kit comprising: (a) conjugated capsular oligosaccharide from *N.meningitidis* serogroup A, in lyophilised form; and (b) one or more further antigens in liquid form, wherein component (b) comprises a saccharide antigen from *Haemophilus influenzae* B and/or wherein the further antigen in component (b) is conjugated capsular oligosaccharide from *N.meningitidis* serogroup C."

VI. The opponent filed a notice of appeal and subsequently withdrew its appeal.

VII. In response to the statement of grounds of appeal, the opponent (respondent) submitted that the opposition division's decision "*was fully justified and we have no further comments at this time*".

VIII. The board issued a summons to oral proceedings accompanied by a communication pursuant to Article 15(1) RPBA informing the parties that the respondent's submission in reply to the statement of grounds of appeal (see section VII above) was understood by the board as an implicit request to dismiss the appeal.

In a further communication pursuant to Article 15(1) RPBA the board set out its preliminary opinion that the subject-matter of claims 1 of the main request and of auxiliary request 1 lacked an inventive step.

IX. Both the appellant and the respondent informed the board that they would not attend the oral proceedings. The appellant also withdrew the request for oral proceedings.

X. Oral proceedings before the board were held on 5 February 2019. The parties were not present or represented, as stated beforehand in writing. At the end of the oral proceedings, the Chair announced the board's decision.

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

D1 WO02/00249 (3 January 2002)

D3 Costantino P. et al., Vaccine (1992), vol. 10, pages 691 to 698

D5 Ravenscroft N. et al., Vaccine (1999), vol. 17, pages 2802 to 2816

D17 Lei Q.P. et al., in Brown F., Corbel M., Griffiths E. (eds): Physico-Chemical Procedures for the Characterization of Vaccines. Dev. Biol. Basel, Karger (2000), vol. 103, pages 259 to 264

XII. The appellant's arguments relevant to the present decision, submitted in writing, may be summarised as follows:

Main request

Novelty (Article 54(2) EPC) - claim 1

Document D1 did not anticipate the claimed subject-matter because feature (a) of the claim was not disclosed directly and unambiguously in that document.

It was necessary to make a triple selection in the embodiment described on page 5, lines 18 to 25 of document D1 to arrive at the claimed subject-matter.

Firstly, it was necessary to select that the MenA antigen referred to in the passage was a capsular saccharide antigen.

Secondly, it was necessary to select the use of a capsular oligosaccharide antigen in the specific embodiment recited on page 5, rather than the polysaccharide antigens described throughout the

description, as the most preferred form of antigen. In order to select this feature the skilled person would have to turn to page 10, lines 20 to 25 of document D1.

Thirdly, it was necessary to select that the MenA antigen in particular was an oligosaccharide as opposed to selecting one or more of the other polysaccharides required in the embodiment on page 5 to be replaced with an oligosaccharide.

Inventive step (Article 56 EPC) - claim 1

Closest prior art

The closest prior art for the subject-matter of the main request was document D17 or document D3, and not document D1 as suggested in the decision under appeal.

The purpose of the invention was the preparation of multivalent vaccines comprising a *Neisseria meningitidis* serogroup A (MenA) antigen. All three documents D1, D3 and D17 had this purpose and therefore it could not be determined on this criterion alone which of the documents was the appropriate choice of closest prior art.

The opposition division incorrectly considered the number of common features between the prior art and the claimed invention before attempting to distinguish between the three prior art documents, based on the similarity of the effect provided by the disclosures in the prior art and the claimed invention - as required by decision T 606/89.

The effect provided by the claimed invention was the increased stability of conjugated MenA oligosaccharide.

Data demonstrating the stability of a MenA conjugate in a liquid tetravalent *Neisseria meningitidis* vaccine containing antigens from serogroups A, C, W and W (MenACWY vaccine) were provided and compared with the stability of a MenA conjugate in a tetravalent MenACWY vaccine in which the MenA conjugate was lyophilised and the further three antigens were in liquid form. The comparison showed that lyophilisation of the MenA conjugate provided superior stability of the MenA conjugate when compared to a vaccine in fully liquid form.

Document D17 was the most promising starting point because it specifically considered the stability of *Neisseria meningitidis* (meningococcal) polysaccharide conjugate vaccines.

Document D1 could not be considered to be the closest prior art *inter alia* because it did not relate to stability and therefore did not demonstrate the same effect as the claimed invention. It also did not give any reason as to why lyophilised MenA antigen was used.

If document D17 was not considered to be the closest prior art because the same effect was not the primary criterion, and the number of differences between the subject-matter of the main request and the prior art documents were considered to be more relevant, then document D1 was still not the closest prior art. This was document D3, because the relevant subject-matter disclosed in document D1 had fewer features in common with the claimed subject-matter than that disclosed in document D3. While document D1 differed from the claimed invention in that the MenA antigen was not disclosed as being (i) conjugated, (ii) capsular and (iii) an oligosaccharide, the subject-matter disclosed

in document D3 seemed to differ by only one feature, namely in that the MenA antigen was not lyophilised.

Technical problem and its solution

The difference between the claimed subject-matter and that disclosed in document D3 or D17 was that, in the kit, the MenA antigen was in lyophilised form, whilst the other antigens of the vaccine were retained in liquid form, whereas in prior art documents D3 or D17 all antigens in the kit were in liquid form.

The effect of this difference was the increased stability of the vaccine.

Therefore, the objective technical problem in view of the disclosure of document D3 or D17 was to provide an improved vaccine in terms of better stability comprising a conjugated MenA antigen.

Obviousness of the claimed solution

Starting from document D17 or D3, the skilled person would not have considered using lyophilised MenA conjugate, whilst retaining some or all of the other antigens in a liquid form, in order to provide a vaccine with improved stability.

Document D1 was the only document that mentioned lyophilisation, but it did not mention the purpose of the lyophilisation of the vaccine components.

Auxiliary request 1

Inventive step (Article 56 EPC) - claim 1

The subject-matter of claim 1 of auxiliary request 1 was inventive for the same reasons as explained for the main request.

Document D17 remained the most appropriate choice of the closest prior art because it related to the same effect as the claimed subject-matter.

If the closest prior art were to be identified primarily based on the number of features in common with the claimed subject-matter, then document D5 was a more appropriate choice as the closest prior art. Document D5 related to meningococcal capsular oligosaccharides used to prepare conjugate vaccines. A pool of MenA oligosaccharides, which had an average degree of polymerisation of 15.7, i.e. a degree which fell within the range claimed in auxiliary request 1, was used for conjugation to the carrier protein CRM_{197}. The only difference between the subject-matter of claim 1 and that of document D5 was the feature that the MenA conjugate was lyophilised.

Therefore, the number of features distinguishing the claimed subject-matter and the disclosure of document D5 (one) was smaller than the number of features distinguishing the claimed subject-matter and the disclosure of either of documents D1 or D3 (at least two) and therefore document D5 was a more appropriate choice as the closest prior art.

Starting from document D5, the skilled person would not have considered producing a multivalent vaccine kit in which the MenA conjugate was lyophilised, whilst some

or all of the other antigens were retained in liquid form, in order to provide a vaccine with improved stability.

XIII. The respondent did not file any arguments during the appeal proceedings.

XIV. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the set of claims of the main request, or, alternatively, on the basis of the set of claims of auxiliary request 1 and a description adapted thereto, or on the basis of the set of claims of auxiliary request 2 and the adapted description filed during the oral proceedings before the opposition division.

The respondent requested that the appeal be dismissed.

Reasons for the Decision

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

2. The opponent filed a notice of appeal and subsequently withdrew its appeal. Accordingly, the opponent is the respondent in these appeal proceedings.

3. The duly summoned parties were neither present nor represented at the oral proceedings. The board decided to continue the proceedings without the parties in accordance with Rule 115(2) EPC and treated them as relying on their written case in accordance with Article 15(3) RPBA.

Main request

Novelty (Article 54(2) EPC) - claim 1

4. The opposition division considered that the claimed subject-matter was not entitled to the claimed priority and that the effective date of the claimed subject-matter was thus the filing date. Therefore, document D1 belonged to the state of the art pursuant to Article 54(2) EPC. This document was considered to anticipate the subject-matter of *inter alia* claim 1 (see decision under appeal, Reasons, points 3.3, 3.4 and 4).

5. The appellant does not contest that the claimed subject-matter is not entitled to claim priority but argues that the feature of the MenA antigen specifically being a conjugated capsular oligosaccharide is not directly and unambiguously disclosed in document D1.

6. The board concurs with the appellant that document D1 does not disclose the subject-matter of claim 1 of the main request.

7. However, the board disagrees with the appellant with regard to the extent of the disclosure of document D1. In the board's view, the reference to "*MenA*" on page 5, line 20 would be understood by the skilled person to refer to "*N. meningitidis* serogroup A capsular polysaccharide", see also page 8, lines 18 to 19 of document D1. This understanding is further supported by page 12, lines 1 to 12 of document D1.

8. Therefore, the board considers that document D1 discloses directly and unambiguously on page 5, lines

18 to 25, a kit comprising conjugated capsular polysaccharide from *N. meningitidis* serogroup A, in lyophilised form, and one or more further antigens in liquid form.

9. In view of the above analysis, the board concludes that the subject-matter of claim 1 fulfils the requirements of Article 54 EPC.

Inventive step (Article 56 EPC) - claim 1

Closest prior art

10. In the decision under appeal, document D1 was considered to be the closest prior art in relation to the subject-matter of claim 1 of auxiliary request 1, because it dealt with the same general problem, i.e. the production of multi-component vaccines and because the relevant subject-matter had the highest number of structural features in common with the claimed subject-matter (see Reasons, point 7.5).

11. The appellant does not dispute that the purpose of the invention is the preparation of multivalent vaccines comprising an antigen from *Neisseria meningitidis* serogroup A (MenA antigen) and that all three documents D1, D3 and D17 relate to this purpose, but submits that it cannot be determined on this criterion alone which of these documents is the most appropriate choice as the closest prior art. Thus, before considering the commonality of technical features, the effect achieved by the claimed invention should be taken into account as agreed by the board in decision T 606/89.

12. According to the established jurisprudence of the Boards of Appeal the closest prior art for assessing inventive step is normally a prior art document which discloses subject-matter conceived for the same purpose or with the same objective as the claimed invention and having the most relevant technical features in common, *i.e.* requiring the minimum of structural modifications (see Case Law of the Boards of Appeal of the European Patent Office, 8th edition 2016, I.D.3.1).

13. In the board's view, contrary to the submissions of the appellant, it cannot be derived from decision T 606/89 that to determine the closest prior art, a distinction should be made between documents based on the actual effect provided by the subject-matter as disclosed in the prior art and the claimed invention before assessing the commonality of technical features. Rather, also in this decision the same criteria set out in point 12, above, are taken into account to establish the closest prior art (see Reasons, point 2).

14. Given that, as agreed by the appellant, the purpose that can be derived from the relevant documents - documents D1, D3 and D17 - is the same as that of the claimed invention, the board will now determine the differences in the technical features (see point 12 above).

15. The kit disclosed in document D1 differs from the claimed kit in respect of just one feature, i.e. in that in the conjugate, the capsular saccharide component from the *Neisseria meningitidis* serogroup A (MenA) is a polysaccharide and not an oligosaccharide (see point 8 above).

16. Document D3 discloses a liquid formulation comprising capsular MenA and MenC oligosaccharides coupled to CRM_{197} (see abstract and page 693, left hand column, third paragraph). This formulation differs from the compounds in the kit as claimed in two aspects, i.e. in that (i) the MenA oligosaccharide is not lyophilised and in that (ii) it is already mixed with the further antigen MenC.

17. Document D17 discloses a liquid tetravalent vaccine comprising polysaccharides from *Neisseria meningitidis* serotypes A, C, W and Y which are individually linked to diphtheria toxoid (see page 259, last paragraph to page 260, second paragraph). This vaccine differs from the compounds in the kit as claimed in that (i) the saccharide component of the MenA conjugate is a polysaccharide and not an oligosaccharide, in that (ii) the conjugate is not lyophilised and (iii) is already mixed with the further antigens.

18. In view of the above analysis the board concludes that document D1 satisfies the established criteria - same purpose and requiring the minimum of structural modifications (see point 12) - to qualify as the closest prior art.

Technical problem

19. The subject-matter of claim 1 differs from the disclosure of document D1 in that the saccharide component of the conjugate is an oligosaccharide (see point 15).

20. There are no submissions in the proceedings by the appellant regarding the technical effect linked to this particular difference, this being due to the fact that

the appellant's line of argument was confined to submitting that either document D3 or D17 was the closest prior art and that the relevant subject-matter disclosed therein differed from the claimed subject-matter in that the MenA antigen was in lyophilised form.

21. Accordingly, the board is of the opinion that starting from document D1 as the closest prior art, the problem to be solved can be seen as that of providing an alternative kit comprising a conjugated capsular saccharide from *Neisseria meningitidis* serogroup A, in lyophilised form, and one or more further antigens in liquid form.

Obviousness of the claimed solution

22. It needs to be established whether or not the skilled person, starting from the teaching in document D1 and faced with the objective technical problem as formulated in the preceding point, would have modified the teaching in the closest prior art document D1 in the light of other teachings in the prior art so as to arrive at the claimed invention.

23. Document D1 already mentions that instead of bacterial polysaccharides, bacterial oligosaccharides, "*which are well known in the vaccine art*", can be used (see page 10, lines 20 to 25).

24. The skilled person working in the field of vaccines is also aware of the disclosure of document D5. This document concerns the development of saccharide-conjugate vaccines against *Haemophilus influenza* type b (Hib) and *Neisseria meningitidis* serogroups A and C. The document discloses that the vaccines consist of

oligosaccharides covalently attached to CRM_{197} and that the preparation of MenA oligosaccharides has an average degree of polymerisation (DP) of 15.7 (see abstract; page 2802, right hand column, lines 1 to 12; page 2803, right hand column, section 2.3 and page 2810, section 3.7).

25. In the board's judgement, the teaching of document D1 (see point 23 above) would have prompted the skilled person to replace the MenA polysaccharide in the kit of document D1 with the MenA oligosaccharide known from document D5. The skilled person would thus have arrived at the claimed invention in an obvious manner.

26. The board concludes from the above analysis that the subject-matter of claim 1 fails to meet the requirements of Article 56 EPC.

Auxiliary request 1

Inventive step (Article 56 EPC) - claim 1

Closest prior art

27. The subject-matter of claim 1 of auxiliary request 1 differs from the subject-matter of claim 1 of the main request in that "*the serogroup A saccharide has an average degree of polymerisation of between 10 and 20*" (see section V).

28. The appellant submitted that document D17 remained the most appropriate choice of closest prior art, but that, if the closest prior art was to be identified based on the document with the greatest number of features in common, then it was document D5 that qualified as the closest prior art. The number of features

distinguishing the claimed subject-matter and that disclosed in document D5 (one) was smaller than the number of features distinguishing the claimed subject-matter and that disclosed in document D1 (at least two).

29. However, in the board's view, the vaccines disclosed in document D5 (see also point 24) differ from the claimed invention in two features rather than one, namely in that (i) the oligosaccharide from *Neisseria meningitidis* serogroup A is not lyophilised and (ii) in that it is already mixed with the further antigens.

30. The kit disclosed in document D1 differs from the claimed invention in that the saccharide component of the MenA conjugate is a polysaccharide and not an oligosaccharide having a certain DP.

31. In the board's view, document D1 is thus also the closest prior art to the subject-matter of claim 1 of auxiliary request 1 because it satisfies the established criteria - same purpose and requiring the minimum of structural modifications (see point 12) - in respect of this invention as well.

Technical problem and its solution, obviousness

32. In the board's view, the analysis set out above for the subject-matter of claim 1 of the main request (see points 22 to 26) applies, *mutatis mutandis*, to the subject-matter of claim 1 of auxiliary request 1. Thus, the skilled person would arrive in an obvious manner at a kit comprising a conjugated capsular oligosaccharide from *Neisseria meningitidis* serogroup A, in lyophilised form, wherein the serogroup A saccharide has an average DP of 15.7 and, thus, would arrive at an embodiment

falling within the scope of claim 1 which defines the serogroup A saccharide as having an average DP of between 10 and 20.

33. Therefore, the subject-matter of claim 1 as a whole fails to meet the requirements of Article 56 EPC.

Auxiliary request 2

34. This request corresponds to the amended form of the patent considered allowable in the decision under appeal.

35. Since the patent proprietor is the sole appellant, the board has no power to review the decision under appeal as regards auxiliary request 2 because of the principle of prohibition of *reformatio in peius* (see decision G 9/92, OJ EPO 1994, 875, Headnote I).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

S. Lichtenvort G. Alt

Decision electronically authenticated