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Datasheet for the decision of 14 February 2019

Case Number: T 0878/15 - 3.3.04

Application Number: 10713516.2

Publication Number: 2411048

IPC: A61K39/095

Language of the proceedings: EN

Title of invention:
Adjuvanting meningococcal factor H binding protein

Applicant:
Novartis AG

Headword:
Factor H binding protein/NOVARTIS

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - main request (yes)

Decisions cited:

Catchword:

-

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Case Number: T 0878/15 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 14 February 2019

Appellant: (Applicant)	Novartis AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Marshall, Cameron John Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 11 November 2014 refusing European patent application No. 10713516.2 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	B. Claes
	L. Bühler

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse European patent application No. 10 713 516.2. The application was published as international application No. WO2010/109323 with the title "*Adjuvanting meningococcal factor H binding protein*".

II. The examining division held that the subject-matter of the claims of the main request and the 1st to 5th auxiliary requests did not involve an inventive step in the light of the disclosure in document D1 representing the closest prior art in combination with the disclosure in document D16 (Article 56 EPC).

Independent claims 1 and 2 of the main request read:

"1. An immunogenic composition comprising two different meningococcal fHBP antigens, both of which are adsorbed to aluminium hydroxyphosphate adjuvant, wherein (i) both of the meningococcal fHBP antigens have an isoelectric point between 5.0 and 7.0, (ii) the aluminium hydroxyphosphate adjuvant has a point of zero charge between 5.0 and 7.0, and (iii) the composition includes a buffer to maintain pH in the range of 5.0 to 7.0.

2. A method for adsorbing two different meningococcal fHBP antigens to an aluminium hydroxyphosphate adjuvant to give an immunogenic composition, wherein (i) both of the meningococcal fHBP antigens have an isoelectric point between 5.0 and 7.0, (ii) the aluminium hydroxyphosphate adjuvant has a point of zero charge between 5.0 and 7.0, and (iii) adsorption of both of

the fHBP antigens takes place at a pH between 5.0 and 7.0 in the presence of a buffer."

Claims 3 to 18 of the main request were dependent on claim 1 and/or claim 2.

III. In the statement of the grounds of appeal the appellant submitted arguments to the effect that the subject-matter of the claims of the requests on file (being the same as those dealt with in the decision under appeal) involved an inventive step. It further submitted an experimental report (D17). Oral proceedings were requested should the board intend to dismiss the appeal.

IV. The rapporteur informed the appellant by telephone of the board's opinion that the subject-matter of the claims of the main request involved an inventive step and that the requirements of Article 56 EPC were fulfilled.

V. Subsequently, the appellant requested that the decision under appeal be set aside and the case be remitted to the examining division either for further prosecution or with the order to grant a patent on the basis of the main request.

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

D1: Anderson *et al.* (2008), Abstracts and poster presentations of the 16th International Pathogenic Neisseria Conference 2008, Abstract P100 (http://neisseria.org/ipnc/2008/Abstracts_poster_presentations_IPNC_2008.pdf)

D16: Lindblad (2004), Immunology and Cell Biology, Vol. 82, pages 497 to 505

Annex (A): Document filed by the appellant during the oral proceedings before the examining division

D17: Experimental report

VII. The appellant's arguments in relation to inventive step of the claimed subject-matter of the main request can be summarised as follows:

The claimed invention was not obvious to the skilled person when combining the teaching in document D1, which represented the closest prior art, with the disclosure in document D16.

Document D1 disclosed vaccine compositions comprising two meningococcal factor H binding protein (fHBP) antigens "adsorbed to AlPO4", whereby the latter was stated to provide enhanced immunogenicity. However, document D1 provided no details on isoelectric points (pI) for the two antigens, the point-of-zero charge (PZC) for the adjuvant, the inclusion of a buffer or the pH of the composition. Nor did it give practical guidance on how the adsorbed formulations could be implemented to achieve the enhanced immunogenicity and therefore lacked an enabling disclosure for the described compositions.

The problem to be solved was thus to provide a real-world practical implementation of the beneficial compositions disclosed in document D1. Alternatively, the problem could be formulated, as the examining

division had done, as the provision of an alternative immunogenic composition.

The examining division was incorrect to find that document D16 disclosed standard methods and parameter values which the skilled person would apply for formulating the disclosed AlPO4 adjuvant vaccines. What document D16 taught the skilled person was that in general for the formulation of aluminium-adjuvanted vaccines, the pI of the antigen should be chosen so that the antigen's charge was opposite to that of the adjuvant.

However, neither document D16 nor any other cited prior art document focused on the seelction of the fHBP antigens in vaccines according to their isoelectric point (pI) in particular ranges or on the selection of an aluminium adjuvant for adsorbing the fHBP antigens in vaccines according to its point-of-zero charge (PZC) in particular ranges. Thus, none of the documents cited suggested choosing a fHBP antigen with a pI within the claimed range of 5.0 to 7.0 (or 5.0 in particular). Document D9, for example, disclosed a vaccine based on a fHBP with a pI of 7.23. Similarly, the cited documents did not teach the skilled person that for the vaccines an aluminium adjuvant should be chosen with a PZC within the claimed range of 5.0 to 7.0 (or 7.0 in particular). Whereas Figure 2 of document D16 indicated an AlPO4 adjuvant with a PZC generally lower than 7, the document did not make any specific proposals on what particular PZC to choose. Document D4, for example, disclosed aluminium hydroxyphosphate with a PZC of 4.0, and document D6 used adjuvants with PZC ranging "*from 8.0 to 4*.7".

Neither document D1 nor document D16 disclosed the inclusion of a buffer in the vaccine, which was not unreasonable given that unbuffered vaccines were known in the prior art. Furthermore, document D16 made the choice of the pH of the vaccine dependent on the pI of antigen and the PZC of the aluminium adjuvant, but it never pointed to choosing a pH within the claimed range of 5.0 to 7.0 or 6.0 in particular.

Document D16 proposed the choice of a particular pH depending on an already selected pI and a PZC.

Document D16 did not imply or make any suggestion that would incline the skilled person to choose the specific combination of parameters referred to by the examining division in the decision under appeal, i.e. a pI of the antigen being 5.0, a PZC being 7.0, vaccine buffering and to choose a pH of 6.0 for the buffer.

Since nothing in documents D1 or D16, or in any other prior art document cited, directed the skilled person towards the specific values specified for the antigen pI, the adjuvant PZC and the buffered formulation pH in claim 1, the subject-matter of claim 1 was not an obvious way of implementing the teaching in document D1.

Thus, the prior art contained no disclosure of how to achieve adsorption of fHBP to an aluminium hydroxyphosphate adjuvant, and the specific ranges specified in claim 1 in relation to the pI for both fHBP antigens, PZC and the buffer pH were not obviously derivable from the prior art. The application, on the other hand, disclosed that these three parameters needed to be considered when formulating fHBP vaccines and that by specifying them in accordance with claim 1

adsorbed vaccine formulations were provided which achieved the advantageous effects reported - but not enabled - by document D1.

The application included adequate supporting data for the claims. Furthermore, the newly filed experimental data (document D17) countered the examining division's argument that the application's data were "*based on just two peptides falling within the claimed range, combined with a single, constant PZC*" and did not "*provide alternative general teaching over a broad range and for any peptide*".

Reasons for the Decision

1. The appeal is admissible.

Main request - Inventive step (Article 56 EPC)

2. The board agrees with the examining division and the appellant that the disclosure in document D1 represents the closest prior art for the purpose of assessing whether or not the claimed subject-matter involves an inventive step by the "problem and solution" approach.

3. Document D1 is a conference abstract relating to vaccines containing meningococcal factor H binding protein (fHBP) antigens. It discloses a study evaluating the immunogenicity of an experimental vaccine containing two recombinant lipidated fHBP (rLfHBP) representing the two sequence subfamilies (A and B) in cynomolgus macaques. Experiments were conducted to evaluate, *inter alia*, the effect of an aluminum phosphate adjuvant (see "Objectives"). It is stated that "*Significantly higher SBA and IgG titers*

were observed with the inclusion of AlPO4 adjuvant" (see "Results") and it is concluded therefrom that "*(2) the immunogenicity of a bivalent vaccine consisting of both rLP2086 subfamily A and subfamily B antigens is enhanced with the inclusion of the aluminium phosphate adjuvant*" (see "Conclusion").

4. Contrary to the disclosure in document D1 - which does not disclose the isoelectric points (pI) of the two subfamily A and B antigens of the immunogenic compositions, the point-of-zero charge (PZC) of the used adjuvant or whether the composition is buffered and at which pH - claim 1 requires that (i) the two meningococcal fHBP antigens of the immunogenic composition adsorbed to the aluminium hydroxyphosphate adjuvant each have a pI between 5.0 and 7.0, (ii) the aluminium hydroxyphosphate adjuvant has a PZC between 5.0 and 7.0 and (iii) the composition includes a buffer to maintain pH in the range of 5.0 to 7.0.

5. The technical effect of this difference is that parameters are now defined which allow it to provide immunogenic compositions with enhanced immunogenicity over the non-adjuvanted compositions as disclosed in document D1. The application does not disclose, and this has not been argued by the appellant either, that the claimed immunogenic compositions have an optimised adsorption compared with any of the composition comprising AlPO4 disclosed in document D1.

6. The technical problem to be solved to be is thus the provision/practical implementation of further/ alternative immunogenic compositions comprising two different meningococcal fHBP antigens which are both adsorbed to aluminium hydroxyphosphate adjuvant.

7. The solution to the problem in accordance with the invention is the choice of the values for the parameters as defined in claim 1.

8. The claimed subject-matter solves the above problem in view of the experiments disclosed in the application as filed (see, for instance, the table on page 31) and as supplemented with later submitted experimental results (see Annex (A) and document D17).

9. The board concurs with the submission of the appellant that the available prior art, including document D16, fails to suggest the skilled person - when addressing the technical problem - the particular choices for the antigens and their pI, the PZC of the aluminium hydroxyphosphate adjuvant and whether to include a buffer and at what pH, let alone a suggest a combination thereof, which the skilled person would get from the combination of the specific features defined in claim 1.

10. Rather, in the context of aluminium adsorption of antigens for use in vaccines, document D16, on page 499, right-hand column, lines 16 to 19, gives the general consideration that: "*The physicochemical mechanisms behind the antigen adsorption itself are complex and depend on the nature of the individual antigen. Some mechanisms may predominate over others.*"

11. For this reason, the particular combination of parameter choices defining the claimed subject-matter would not have been obvious to the skilled person. Accordingly, the subject-matter of the claims of the main request involves an inventive step. The requirements of Article 56 EPC are hence fulfilled.

Remittal to the examining division for further prosecution

12. The sole reason for refusing the application was that the claimed subject-matter, including that of the claims of the main request, lacked inventive step (Article 56 EPC). The examining division has not expressed an opinion on the other EPC requirements for the application to be granted. Under these circumstances, and in view of the appellant's corresponding request (see section V), the board considers it appropriate to remit the case to the examining division for further prosecution in accordance with Article 111(1), second sentence, EPC.

13. As the board complied with the appellant's main procedural request, it was in a position to decide the case without oral proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division for further prosecution.

The Registrar: The Chair:

S. Lichtenvort G. Alt

Decision electronically authenticated