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Datasheet for the decision of 25 June 2015

Case Number: T 1125/13 - 3.3.04

Application Number: 05740675.3

Publication Number: 1755662

IPC: A61K39/095, A61K47/48, G01N33/50

Language of the proceedings: EN

Title of invention:
Combined meningococcal conjugates with common carrier protein

Patent Proprietor:
Novartis AG

Opponent:
GlaxoSmithKline Biologicals SA/ opposition withdrawn

Headword:
Conjugate vaccine with common carrier/NOVARTIS

Relevant legal provisions:
EPC Art. 56, 113(2)
EPC R. 115(2)
RPBA Art. 15(3)

Keyword:
Main request - inventive step (no)
Auxiliary requests - not taken into account

Decisions cited:
R 0014/10, T 0629/90, T 0382/96

Catchword:

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Case Number: T 1125/13 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 25 June 2015

Appellant: (Patent Proprietor)	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 Opposition Division of the European Patent Office posted on 19 February 2013 revoking European patent No. 1755662 pursuant to Article 101(2) and Article 101(3)(b) EPC.**

Composition of the Board:

Chairwoman G. Alt
Members: R. Morawetz
M. Blasi

Summary of Facts and Submissions

I. The appeal of the proprietor ("appellant") lies against the decision of the opposition division to revoke European patent No. EP 1 755 662. The patent at issue has the title "Combined meningococcal conjugates with common carrier protein".

II. The opposition division decided *inter alia* that the subject-matter of the main request (claims as granted) and of auxiliary requests 1 and 3 to 8 lacked novelty and that the subject-matter of auxiliary request 2 lacked inventive step.

III. With its statement of grounds of appeal the appellant maintained the claims as granted as its main request. It also submitted five sets of auxiliary requests: B, C and D; 1 to 6; 1B to 6B; 1C to 6C and 1D to 6D.

Claims 1 and 4 of the main request read:

1. "A composition for immunising a patient against a disease caused by *Neisseria meningitidis* comprising at least two of: (a) a conjugate of (i) the capsular saccharide of serogroup A *N. meningitidis* and (ii) a carrier protein; (b) a conjugate of (i) the capsular saccharide of serogroup C *N.meningitidis* and (ii) a carrier protein; (c) a conjugate of (i) the capsular saccharide of serogroup W135 *N.meningitidis* and (ii) a carrier protein; (d) a conjugate of (i) the capsular saccharide of serogroup Y *N.meningitidis* and (ii) a carrier protein, characterised in that (1) at least two of said conjugates (a), (b), (c) and (d) use the same carrier protein ('the common carrier'), and (2) the composition includes the common carrier in an unconjugated form,

wherein the concentration of the unconjugated common carrier is less than 10 µg/ml.

4. The composition of any preceding claim, wherein each of the meningococcal conjugates is conjugated to a common carrier selected from: diphtheria toxoid; tetanus toxoid; CRM197; and protein D from *H. influenzae*."

IV. In relation to the auxiliary requests, the appellant submitted in the statement of grounds of appeal in points 1.7 to 1.9 *inter alia* that (i) with regard to the first auxiliary request (which had been the first auxiliary request in the first instance proceedings) "the opposition division failed to establish that D3 or D6 discloses unconjugated carrier protein in solution", (ii) "the second to sixth auxiliary requests contain other novel features compared to D3 and D6", and (iii) the remaining auxiliary requests of the "B" series, the "C" series and the "D" series incorporated additional inventive features into the claims.

The appellant further submitted in point 2.19 of the statement of grounds of appeal that "the first auxiliary request (and related requests AR1B, AR1C and AR1D) is therefore novel over D3", and in point 2.28 that "D6 does not destroy the novelty of the main request (and related requests ARB, ARC, and ARD)".

In point 2.29 of the statement of grounds of appeal the appellant submitted in relation to the novelty of the claimed subject-matter that "In the event that the Board agrees with the opposition division that the main and first auxiliary requests lack novelty over D3 and/ or D6, then the second to sixth auxiliary requests are novel over these documents because of their additional

features". Finally, immediately after consideration of the inventive step of the subject-matter of the main request, it is stated in a heading preceding point 3.20 that "The B, C and D series of auxiliary requests are also inventive".

V. The opponent ("respondent") filed a response to the statement of grounds of appeal.

VI. With its letter of 7 April 2015 the respondent withdrew its opposition.

VII. In a communication pursuant to Article 15(1) RPBA, dated 1 June 2015, the board informed the appellant about some of its preliminary views. With respect to the sets of claims which had been filed by the appellant as its auxiliary requests, the board stated *inter alia* that the "order in which the appellant wishes these requests to be dealt with by the board is not clear". Furthermore, the board gave an example showing why it considered the order of the requests to be unclear and pointed out that it was the party's responsibility to indicate the order of its requests (see point 21 of the communication).

VIII. Oral proceedings before the board were held on 25 June 2015. The duly summoned appellant was not represented as announced in its letter of 7 May 2015. At the end of the oral proceedings the chairwoman announced the board's decision.

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

D1 WO 02/058737

D3 WO 2004/067030

D6 WO 03/007985

D17 Reddin K.M. et al., FEMS Immunology and Medical Microbiology (2001), vol. 31, pages 153-162

D18 WO 02/00249

D19a AU 199877730

D31 WO 00/56360

X. The appellant's arguments submitted in writing may be summarised as follows:

Admission of documents D28 to D31

Documents D28 to D31 should be admitted into the proceedings because they were a direct response to the opposition division's decision that carrier suppression had not been demonstrated in the prior art.

Main request

Inventive step (Article 56 EPC)

The purpose of the invention was the provision of multivalent meningococcal conjugate vaccines. The effect of the invention was the successful immunisation against the relevant meningococcal serogroups with no signs of carrier suppression. This effect was demonstrated in paragraph [0135] of the patent. Document D1 could not represent the closest prior art because it did not relate to the avoidance of carrier suppression.

Documents D17, D18, D19a or D31, all of which related to carrier suppression, were closer prior art than document D1. Starting from these documents, the skilled person would not have been led to the invention because they all recommended using multiple carrier proteins to avoid carrier suppression. In contrast, the present invention was based on the use of a common carrier protein.

The invention could not be reached starting from document D1 either. Contrary to the finding of the opposition division, the technical effect of avoiding carrier suppression had been shown for the subject-matter of the main request.

XI. The (former) respondent's arguments submitted in writing may be summarised as follows:

Admission of documents D28 to D31 and D33 to D35

Documents D28 to D31 represented late filed evidence by the appellant for the existence of carrier suppression which did not advance the debate and should not be admitted. Documents D33 to D35 should be admitted if documents D28 to D31 were admitted.

Main request

Inventive step (Article 56 EPC)

Document D1 was a good candidate for the closest prior art. It related to a tetravalent conjugated meningococcal vaccine in which diphtheria toxoid (Dt) was the common carrier of the four conjugates.
It was thus related to the same purpose as the

invention, which was the provision of an effective multivalent meningococcal vaccine and this purpose was achieved by the technical effect of avoiding carrier suppression.

The patent invited the reader to infer that, because good immunogenicity was seen, there could not have been any carrier suppression. Document D1 disclosed in Tables 2 and 3 data which were comparable to those in Table 1 of the patent and from which therefore exactly the same inference could be made.

None of documents D17, D18, D19a and D31 related to a tetravalent conjugated meningococcal vaccine with a common carrier.

If document D1 was taken as the closest prior art, then the problem to be solved was how to implement its teaching.

XII. The appellant requested in writing that the decision under appeal be set aside and that the opposition be rejected, or in the alternative that a patent be granted on the basis of one of the auxiliary requests filed with the statement of grounds of appeal.

Reasons for the Decision

1. With its letter of 7 April 2015 the respondent withdrew its opposition. It thus ceased to be a party to the appeal proceedings. The appeal proceedings were not affected by the withdrawal of the opposition. The board was still obliged to examine the substance of the opposition division's decision in order to ascertain if it was to be set aside and whether the patent, on the

basis of the appellant's requests, met the requirements of the EPC. In so doing, under Article 114(1) EPC the board was able to take account of the submissions and evidence filed by the respondent prior to its withdrawal of the opposition (see also T 629/90, OJ EPO 1992, 654, Headnote).

2. The duly summoned appellant did not attend the oral proceedings, as announced in its letter of 7 May 2015. In accordance with Rule 115(2) EPC and Article 15(3) RPBA the oral proceedings took place in the absence of the appellant, who was taken to rely on its written submissions.

Admission of documents D28 to D31 and D33 to D35

3. Documents D28 to D31 were filed by the appellant with its statement of grounds of appeal. Documents D33 to D35 were filed by the former respondent with its reply to the statement of grounds of appeal. Document D31 concerns bi- and trivalent *N. meningitidis* conjugate vaccines. The board decided to admit document D31 into the appeal proceedings as it was considered to have the same purpose as the present invention and thus to be of relevance to the issue to be decided (see below, points 5 to 16).

4. Documents D28, D30 and D33 to D35 were not directly related to the issues to be decided. Therefore, the board did not need to decide whether to admit these documents into the appeal proceedings.

Main request

Inventive step (Article 56 EPC)

Closest prior art

5. The closest prior art for assessing inventive step is normally a prior art document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common (see also Case Law of the Boards of Appeal of the EPO, 7th edition 2013, section I.D.3.1).

6. As can be derived from paragraph [0001] of the patent which states "This invention concerns vaccines against *Neisseria meningitidis*. In particular, it corns [*sic*] vaccines based on conjugated capsular saccharides from multiple meningococcal serogroups", the purpose of the present invention is the provision of a vaccine against *Neisseria meningitidis* (*N. meningitidis*), in particular a tetravalent vaccine based on conjugated capsular saccharides of those meningococcal serogroups which are most relevant and already present in commercially available vaccines, i.e. A, C, Y, and W135 (see paragraphs [0002] and [0003] of the patent).

7. Document D1 discloses (see example 6) a tetravalent meningococcal conjugate vaccine comprising capsular polysaccharides from serogroups A, C, Y, and W135 of *N. meningitidis* separately conjugated to diphtheria toxoid (Dt) as the common carrier. In Example 9 the vaccine is shown to be immunogenic in young healthy adults (see Table 2 of document D1) and in toddlers (see Table 3 of document D1).

8. Document D17 concerns the use of *Bordetella pertussis* fimbriae as carrier proteins in a monovalent *N. meningitidis* serogroup C conjugate vaccine (see abstract).

9. Document D18 discloses a combination vaccine comprising *N. meningitides* type A and type C capsular polysaccharides conjugated to protein D from *Haemophilus influenza* (*H. influenza*) as the carrier (see example 2(i)).

10. Document D19a discloses multivalent carrier-conjugated *Streptococcus pneumoniae* vaccines (see page 5, first paragraph).

11. Document D31 discloses bi- and trivalent *N. meningitides* conjugate vaccines wherein the carrier is protein D from *H. influenzae* (see for example page 25, lines 17 to 20).

12. In the board's view, with the exception of document D19a, which is concerned with *Streptococcus pneumoniae* vaccines, all of the above-mentioned documents have the same purpose as the present invention, namely the provision of a vaccine against *N. meningitidis*.

13. The appellant submitted that the purpose of the invention was the avoidance of carrier suppression and that this was not mentioned in document D1.

13.1 However, the avoidance of carrier suppression is not to be considered as the purpose of the invention, which is, as stated in point 6 above, the provision of a vaccine against *N. meningitidis.* Rather, the avoidance of carrier suppression is necessary to achieve this purpose.

13.2 Moreover, the board considers that the avoidance of carrier suppression is implied by the immunogenicity data provided in example 9 of document D1 in the same way as it is taught to be implied in paragraph [0135] of the patent summarising the immunogenicity data of the tested CRM197-conjugated meningococcal ACWY vaccines shown in Table 1 of the patent.

14. As to the common relevant technical features, only document D1 discloses a tetravalent conjugated vaccine with a common carrier, namely diphtheria toxin, which is also one of the carriers according to the patent (see paragraph [0024] or claim 4).

15. Thus, in accordance with the criteria established by the case law (see point 5 above), document D1 represents the closest prior art document.

16. For these reasons, the appellant's arguments based on any of documents D17, D18, D19a or D31 as closest prior art fail.

Technical problem

17. One of the embodiments encompassed by the subject-matter of claim 1 is the use of diphtheria toxin as the common carrier (see dependent claim 4). This embodiment of claim 1 differs from the disclosure of document D1 in that the concentration of the unconjugated common carrier present in the composition is explicitly indicated as follows "and (2) the composition includes the common carrier in an unconjugated form, wherein the concentration of the unconjugated common carrier is less than 10 µg/ml".

18. According to the appellant, the effect linked to this difference was the avoidance of carrier suppression. In this context the appellant relied on the statement in paragraph [0135] of the patent saying that no evidence of carrier suppression was seen in clinical trial V59P2.

18.1 However, in this clinical trial only one single tetravalent vaccine was used, and the unconjugated carrier CRM197 was present at a concentration of less than 2 µg/ml (see paragraphs [0131] to [0135]). Other concentrations of unconjugated carrier were not tested. Therefore, there is no evidence in the patent, in particular not in Table 1 of the patent showing the results of the V59P2 trial, on the basis of which a link could be established between the claimed range of concentration of unconjugated carrier protein and the absence of carrier suppression. The board is therefore not convinced by the appellant's submission.

19. Accordingly, the board considers that no technical effect over and above the effect shown for the vaccine composition in document D1, i.e. immunogenicity, can be attributed to the claimed vaccine composition considered here (see point 17 above). Therefore, the problem to be solved is formulated as the provision of an alternative multivalent meningococcal conjugate immunogenic composition.

Obviousness

20. The skilled person faced with the problem formulated above would have been aware of the guidance provided by document D1. Example 5 of document D1 teaches how to prepare monovalent conjugates of *N. meningitidis* serogroup A, C, W-135, and Y capsular polysaccharides

with diphtheria toxoid protein. The conjugates were purified after conjugation of the polysaccharide to the carrier protein (see paragraph [0062]). The purity of the conjugates was determined by measuring the amount of unbound protein by capillary electrophoresis (see paragraph [0063]). Example 6 of document D1 discloses how the serogroup A, C, W-135, and Y polysaccharide-diphtheria toxoid conjugates were combined to yield a tetravalent meningococcal vaccine. The skilled person following this guidance would thus have arrived at an immunogenic composition comprising meningococcal saccharides of serogroup A, C, W-135, and Y conjugated to a common carrier and containing some residual amounts of unbound carrier. The board considers that the upper limit chosen for the amount of residual carrier present in the composition according to claim 1 ("less than 10 µg/ml"), in the absence of any technical effect linked to it, represents an arbitrary value which cannot support any inventive step in view of the teaching of document D1.

21. In view of the above considerations, the subject-matter of claim 1 is considered to be obvious from the teaching of document D1. The main request fails to meet the requirements of Article 56 EPC and is not allowable.

Basis of the decision (Article 113(2) EPC)

22. Pursuant to Article 113(2) EPC the board decides upon a European patent application or patent only in the text submitted to it, or agreed, by the applicant or the proprietor of the patent. Enshrined in this provision is the principle of party disposition, which implies that it is the applicant's or patentee's responsibility to define the subject-matter of the application or the

patent. This responsibility cannot be shifted to the board or other parties to the proceedings. In relation to the established system of main and auxiliary requests in the proceedings before the EPO, this means that the applicant or patentee must indicate the order of preference for each set of claims when filing alternative sets (see also R 14/10, Reasons 5.2 and 5.3; T 382/96, Reasons 5.2, neither decision published in the OJ EPO).

23. The appellant submitted the following five sets of auxiliary requests with the statement of grounds of appeal: B, C and D; 1 to 6; 1B to 6B; 1C to 6C and 1D to 6D (see section III above). Thus, the appellant has not presented its claim requests consecutively numbered in descending order of preference, but has filed different "series" of requests which have no discernible order.

23.1 The particular order in which these requests should be considered by the board can also not be deduced from the explanations provided by the appellant in the statement concerning the various features incorporated into these auxiliary requests (see section IV above).

23.2 And, while the submissions of the appellant in the context of novelty appear to imply that auxiliary request 1 is to be considered after the main request, the submissions in the context of inventive step seem to imply that it is auxiliary request B that should be considered after the main request (see section IV above).

23.3 Hence, the order in which the appellant wishes these claim requests to be considered by the board is not clear. As a result the board does not know what the

text is upon which the patent proprietor wants to have a decision taken. It is in particular not clear whether auxiliary request B is higher-ranking than auxiliary request 1 and whether auxiliary request 1B is higher-ranking than auxiliary request 2.

24. The board informed the appellant prior to the oral proceedings that the order of the submitted claim requests was not clear (see section VII above), and thus gave it the possibility to clarify its requests. However, no submission was received in reply to the board's communication and no later clarification could be obtained due to the appellant's non-attendance at the oral proceedings. The appellant's statement of grounds of appeal thus remained the sole relevant submission in this respect.

25. As it was the appellant's responsibility to indicate the order of its claim requests, the board could only proceed as far the order of the requests was clear to it. It cannot be for the board to speculate which of the various sets of claim requests the appellant might prefer, or to choose the order which might seem suitable. That would run counter to the principle of party disposition and undermine confidence in the objectivity and impartiality of the board.

26. Accordingly, the board dealt with the appellant's main request but, as it was not in a position to establish which of the auxiliary requests should follow, it had no other choice than to ignore them. Hence, the sole request to be considered pursuant to Article 113(2) EPC was the main request.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated