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**Datasheet for the decision  
of 20 July 2020**

**Case Number:** T 0870/14 - 3.3.04

**Application Number:** 08075538.2

**Publication Number:** 1961426

**IPC:** A61K39/095, A61K39/102,  
A61K39/09

**Language of the proceedings:** EN

**Title of invention:**  
Combined meningitis vaccines

**Patent Proprietor:**  
GlaxoSmithKline Biologicals SA

**Opponent:**  
Glaxo Smithkline Biologicals S.A. (opposition withdrawn)

**Headword:**  
Meningococcal Hib vaccine/GLAXOSMITHKLINE

**Relevant legal provisions:**  
EPC Art. 56

**Keyword:**  
Main request, auxiliary requests 1 to 8: inventive step - (no)

**Decisions cited:**

T 0967/97, T 1742/12

**Catchword:**



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Case Number: T 0870/14 - 3.3.04

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.04**  
**of 20 July 2020**

**Appellant:** GlaxoSmithKline Biologicals SA  
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**Decision under appeal:** **Decision of the Opposition Division of the  
European Patent Office posted on 14 April 2014  
revoking European patent No. 1961426 pursuant to  
Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairwoman** G. Alt  
**Members:** D. Luis Alves  
M. Blasi

## Summary of Facts and Submissions

- I. The appeal by the patent proprietor (appellant) concerns the decision of the opposition division to revoke European patent No. 1 961 426, entitled "*Combined meningitis vaccines*". The patent in suit was granted on the basis of European patent application No. 08 075 538.2, a divisional application of European patent application No. 04 791 703.4. The latter had been filed as an international application published as WO 03/007985 and claimed priority from two earlier applications, GB 0 323 102.4, filed on 2 October 2003, and GB 0 412 052.3, filed on 28 May 2004.
- II. An opposition had been filed invoking the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), under Article 100(a) EPC, as well as the grounds under Article 100(b) and (c) EPC.
- III. The decision under appeal dealt with sets of claims of a main request and of auxiliary requests 1 to 8. The opposition division held that neither the main request nor auxiliary requests 1 to 3 complied with the requirements of Article 123(2) EPC, because the subject-matter of claim 6 of each of those requests extended beyond the content of the application as filed. The same applied to auxiliary request 4 with respect to the subject-matter of claim 1. As for auxiliary requests 5 to 8 the opposition division held *inter alia* that the claimed subject-matter did not comply with the requirements of Article 56 EPC.
- IV. With the statement of grounds of appeal, the appellant filed sets of claims of a main request and of auxiliary

requests 1 to 8, all respectively identical to the ones forming the basis of the decision under appeal.

- V. The opponent (respondent) filed a reply to the statement of grounds of appeal and subsequently withdrew its opposition.
- VI. In the course of the appeal proceedings, the appellant withdrew its request for oral proceedings and requested a decision on the basis of the written submissions.
- VII. The **main request** contains six independent claims.

Claim 1 reads:

"1. An aqueous immunogenic composition which, after administration to a subject, is able to induce an immune response that is (a) bactericidal against at least serogroup W135 of *N.meningitidis* and (b) protective against *H.influenzae* type b disease, wherein the composition comprises:  
(i) a conjugated serogroup W135 capsular saccharide antigen; and  
(ii) a conjugated *H.influenzae* type b ('Hib') capsular saccharide antigen;  
and wherein the serogroup W135 saccharide is conjugated to a diphtheria toxoid."

Independent claim 6 differs from claim 1 in that the last feature "and wherein ..." is replaced as follows:

"and wherein the serogroup W135 saccharide is conjugated to a CRM197 diphtheria toxin mutant, and the composition comprises  $\leq 30\mu\text{g}$  meningococcal saccharide per dose".

Claims 1 and 6 of **auxiliary request 1** differ from those of the main request in that the composition is specified to "essentially consist of" the components (i), (ii) and an additional component (iii). Claim 6 further differs from claim 6 of the main request in respect of the last feature. Claims 1 and 6 of auxiliary request 1 thus read as follows (additions underlined; deletions struck through):

"1. An aqueous immunogenic composition which, after administration to a subject, is able to induce an immune response that is (a) bactericidal against at least serogroup W135 of *N.meningitidis* and (b) protective against *H.influenzae* type b disease, wherein the composition ~~comprises~~ consists essentially of:  
(i) a conjugated serogroup W135 capsular saccharide antigen; and  
(ii) a conjugated *H.influenzae* type b ('Hib') capsular saccharide antigen; and  
(iii) conjugated capsular saccharide antigens from serogroups C and Y, and optionally A;  
and wherein the serogroup W135 saccharide is conjugated to a diphtheria toxoid.

6. An aqueous immunogenic composition which, after administration to a subject, is able to induce an immune response that is (a) bactericidal against at least serogroup W135 of *N.meningitidis* and (b) protective against *H.influenzae* type b disease, wherein the composition ~~comprises~~ consists essentially of:  
(i) a conjugated serogroup W135 capsular saccharide antigen; and  
(ii) a conjugated Hib capsular saccharide antigen; and  
(iii) conjugated capsular saccharide antigens from serogroups C and Y and, optionally, A;

and wherein ~~the serogroup W135 saccharide is all~~  
serogroups are conjugated to a CRM197 diphtheria toxin  
mutant, and the composition comprises  $\leq 30\mu\text{g}$   
meningococcal saccharide per dose."

Claim 1 of **auxiliary request 2** differs from that of the  
main request in that the composition is further defined  
by the following additional feature: "and (iii) does  
not comprise one or more polypeptide antigens from  
serogroup B of *N.meningitidis*".

Claim 1 of **auxiliary request 3** differs from that of the  
main request in that the composition is specified to  
comprise both the feature (iii) added to auxiliary  
request 1 and the feature added to auxiliary request 2  
(as feature (iv)).

**Auxiliary request 4** contains a single independent  
claim, which is identical to claim 6 of auxiliary  
request 1.

**Auxiliary requests 5 to 8** correspond to the main  
request and auxiliary requests 1 to 3, respectively,  
wherein independent claim 6 has been deleted.

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

D2: WO 02/00249

D5: WO 02/080965

D6: WO 03/007985

D7: Molrine, Deborah C. *et al*, Ann. Intern. Med.,  
vol. 123, 1995, pages 828-834.

D9a: Granoff, Dan M. *et al*, "Meningococcal Vaccines",  
Vaccines, ed. Stanley A. Plotkin and Walter A.  
Orenstein, 2004, pages 959-987.

D10: Zimmer, Shanta M. *et al*, Expert Opin.  
Pharmacother., vol. 5(4), 2004, pages 855-863.

D11: Foster, Caroline *et al*, Expert Opin. Investig.  
Drugs, vol. 11(8), 2002, pages 1051-1060.

D13: WO 02/058737

IX. The appellant's arguments relevant to this decision may  
be summarised as follows:

*Main request and auxiliary requests 1 to 3 and 5 to 8*

These submissions were made under the heading of  
auxiliary request 1 but are equally applicable to all  
the requests above.

*Inventive step - claim 1*

*Closest prior art*

For compositions which do not include MenB polypeptide  
antigens, such as those specified in claim 1 of  
auxiliary request 1, the closest prior art was  
represented by either document D6 or document D13.  
Document D7, held by the opposition division to  
represent the closest prior art, did not disclose a  
bactericidal response to serogroup W135. It was  
therefore not directed to the same purpose and effect  
as the claimed invention. This was however addressed in



each of document D6 and document D13, which therefore also qualified as the closest prior art.

The opposition division selected the closest prior art by first considering the number of features in common with the claimed invention instead of the purpose and effect. It also considered the technical field and technical effect, but none of these considerations resulted in document D7 being closer than either of documents D6 and D13. Indeed, all the cited documents belonged to the same technical field as the invention.

As for the technical effect, the opposition division first assessed what was in its view the technical effect demonstrated in the patent; however, this was not an appropriate criterion for selecting the closest prior art.

Additionally, whereas documents D6 and D13 were published shortly before the priority date, in 2003 and 2002, respectively, document D7 was published in 1995.

*Technical effect and objective technical problem*

The claimed compositions differed from those disclosed in either of documents D6 and D13 on account of the presence of Hib saccharide, in the form of a conjugate. The effect of this difference was an improved bactericidal immune response against W135 without significant immune interference. The objective technical problem to be solved was the provision of "*a further immunogenic meningococcal conjugate composition that gives an improved bactericidal immune response against W135 serogroup without significant immune interference*" (point 3.23 of the statement of grounds of appeal).

Should document D7 be held to represent the closest prior art, the claimed compositions differed therefrom in that meningococcal saccharides were provided in conjugated form.

The opposition division had not taken into account the effects achieved by the invention compared with those disclosed in document D7, which did not show a bactericidal response against any of serogroups C, W135 and Y, in the presence of a Hib conjugate. The patent showed, by comparing the response to compositions 2 and 3 (tables on pages 26 and 27), an increase in bactericidal response against serogroup W135 for a combination of MenA, C, W135 and Y saccharide conjugates with a Hib saccharide conjugate. Additionally, the responses to the other serogroups were maintained or improved by the addition of Hib saccharide conjugate to the composition. Thus, the effect achieved by the claimed compositions was an improved bactericidal MenW135 response and good serogroup A, C and Y responses, without significant immune interference.

The objective technical problem was the provision of "*a Men(A)CWY composition that gives an improved bactericidal immune response against W135 serogroup and good serogroup A, C and Y responses, without significant immune interference*" (point 3.49 of the statement of grounds of appeal).

#### *Obviousness*

Starting from either of documents D13 and D6, the skilled person had no incentive to combine the tetravalent MenACW135Y conjugate composition disclosed

therein with a Hib saccharide conjugate. The prior art did not provide any incentive to make such a combination with the expectation of achieving an improved bactericidal response against serogroup W135 without significant immune interference.

Starting from the disclosure in document D7, the skilled person had no incentive to replace the MenA, C, W135 and Y polysaccharide antigens with conjugated saccharides. Furthermore, the skilled person would not have reasonably expected such a combination to result in the effects stated above.

While the skilled person would have been aware of the advantages of conjugation in MenACW135Y vaccines, in view of documents D13 and D10, they would also have been aware of the problem of immune interference, for example from document D2 (page 1, lines 7 to 11). The skilled person would thus have been concerned that combining different conjugates in a single composition would affect the immunogenicity of the individual conjugates. None of documents D7, D13 or D6 showed that satisfactory immune responses could be achieved in the presence of Hib saccharide conjugate.

*Auxiliary request 4*

*Inventive step - claim 1*

The line of argument with respect to auxiliary request 1 also applied to this request. In particular the claimed compositions were further characterised by the carrier CRM197 and the amount of saccharide, which were features present in the compositions demonstrated in the patent to have the effects listed above (compositions 2 and 3 in the example in the patent).

- X. The (former) respondent's arguments relevant to this decision may be summarised as follows:

*Main request, auxiliary requests 1 to 3 and 5 to 8*

These submissions were made under the heading of auxiliary request 1 but are equally applicable to all the requests above.

*Inventive step - claim 1*

*Closest prior art*

Document D7 related to the same purpose as it also disclosed a HibMenACWY composition and aimed to induce a protective immune response. The composition resulted from combining two vaccines, which were licensed and thus must have had the bactericidal and protective activity required by the claims. Thus, the composition disclosed in document D7 was expected to achieve a bactericidal and protective response. The compositions disclosed in each of document D6 and document D13, on the other hand, comprised meningococcal conjugates but did not contain Hib antigen. Thus, they did not represent the closest prior art.

*Objective technical problem and obviousness*

Both document D6 and document D13 already demonstrated bactericidal activity for MenW135 saccharide conjugate. The results in the patent did not support an improvement in bactericidal response resulting from combining a Hib conjugate with the meningococcal conjugates.

Starting from document D7 and taking the objective technical problem to be that formulated by the opposition division, the claimed solution was obvious for the following reasons.

Conjugation would have been obvious, for example from document D13. This document disclosed tetravalent conjugate compositions using diphtheria toxoid as the carrier and reported that good results were achieved in mice as well as in a clinical trial (pages 13, 18 to 19 and 21). It provided reasons for the skilled person to use conjugated rather than plain polysaccharide (paragraph 8).

The solution in the claims was also obvious because the advantages of conjugate vaccines over plain polysaccharide vaccines were known, as demonstrated in documents D8 (page 251), D9a (page 980), D10 (page 858) and D11 (page 1051, "*Introduction*" and page 1055).

An incentive to use conjugates instead of plain polysaccharides was additionally provided in further documents. For example document D2 disclosed successful results of clinical trials using a combination of Hib conjugate and MenA and MenC conjugates and suggested adding further meningococcal conjugates (example 3 and page 3, lines 23 to 33). In addition document D5 disclosed combinations of conjugates of Hib, MenC and MenY saccharides (page 5, lines 1 to 8 and 10 to 18). These documents demonstrated that it was feasible to provide the Hib and meningococcal conjugates in the same composition without experiencing interference.

*Auxiliary request 4*

These submissions were made under the heading of claim 6 of auxiliary request 1.

*Inventive step - claim 1*

This subject-matter would also have been obvious from a combination of the teachings of documents D7 and D13. Document D13 disclosed, in a clinical trial, the use of a dose of 4 µg of each meningococcal saccharide, thus 16 µg in total (paragraph 78). The use of CRM197 as the carrier protein would have been obvious as well because it was just a mutant of diphtheria toxoid, the carrier used in the examples, and it was already mentioned as an alternative carrier in this same document (paragraph 27).

- XI. The appellant 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, or alternatively, of one of auxiliary requests 1 to 8, all filed with the statement of grounds of appeal.

**Reasons for the Decision**

1. The appeal is admissible as it complies with the requirements specified in Articles 106 to 108 EPC and the further provisions referred to in Rule 101(1) EPC.
2. In view of its withdrawal of the opposition, the respondent ceased to be a party to the appeal proceedings as regards substantive issues. Other issues

for which the respondent would have remained a party to the proceedings did not arise in the present case.

3. As the impugned decision resulted in the revocation of the patent, the withdrawal of the opposition had no procedural consequences for the appeal proceedings. The board must still examine the opposition division's decision in order to ascertain if it is to be set aside and whether the patent, with account being taken of the amendments made by the appellant in the form of the main request or auxiliary requests 1 to 8, and the invention to which it relates, meet the requirements of the EPC. In so doing the board may take into account the submissions and evidence filed by the respondent prior to its withdrawal of the opposition (see for example decision T 629/90, OJ EPO 1992, 654, point 2.2 of the Reasons).
4. In the decision under appeal the opposition division held, in addition to their finding that the claims lacked an inventive step, that claim 6 of the main request and auxiliary requests 1 to 3 as well as claim 1 of auxiliary request 4 did not comply with the requirements of Article 123(2) EPC. The present decision does not deal with this aspect in view of the board's negative decision in relation to inventive step.
5. The patent in suit concerns compositions for immunisation against meningitis caused in particular by *Neisseria meningitidis* and *Haemophilus influenzae* type B, in particular compositions comprising capsular saccharides from these bacteria. In this decision the board will in some instances refer to these as meningococcal saccharides and Hib saccharides, respectively. Accordingly, a conjugate of serogroup

W135 capsular saccharide antigen of *N. meningitidis* is also referred to as "conjugated MenW135 saccharide" or "MenW135 saccharide conjugate" in the following. Abbreviations to "MenACWY" apply accordingly to saccharides of serogroups A, C, W and Y of *N. meningitidis*. Conjugate of *H. influenzae* type b capsular saccharide antigen is also referred to as "conjugated Hib saccharide" or "Hib saccharide conjugate" in the following.

*Main request and auxiliary requests 1 to 3 and 5 to 8*

6. Independent claims 1 to 5 of the main request and auxiliary requests 1 to 3 are identical to those of auxiliary requests 5 to 8, respectively (see section VII.).
7. Claim 1 of auxiliary request 1 is directed to a composition "consisting essentially of" individually conjugated capsular saccharides of MenW135, C and Y, as well as Hib. As such, this composition falls within claim 1 of the main request as well as that of auxiliary requests 2 and 3 and 5 to 8.

In the following, it is this subject-matter that is being analysed when the board refers to claim 1.

8. In the decision under appeal the opposition division concluded that 28 May 2004 was the valid priority date (page 7 of the decision). This has not been contested in the appeal proceedings.

Thus, documents D9a and D10, referred to below, belong to the state of the art according to Article 54(2) EPC.



*Inventive step*

*The decision under appeal*

9. The opposition division held that, in respect of auxiliary request 1 before it, the subject-matter of claim 1 lacked an inventive step with regard to document D7, considered to represent the closest prior art, in combination with the teaching of either document D13 or document D10.
  
10. The appellant disputes this decision on several accounts: the disclosure of document D7 does not constitute the closest prior art, the opposition division incorrectly formulated the problem by not having taken into account the effect provided by the composition, and the skilled person had no incentive to replace the meningococcal saccharides with the respective conjugates and yet still provide them in a composition with *H. influenzae* saccharide conjugate.

*The closest prior art*

11. Document D7 concerns the immune response to conjugated versus unconjugated polysaccharide vaccines (see title as well as "*Objective*"). For the study, patients were administered a composition comprising unconjugated polysaccharides from *N. meningitidis* serogroups ACYW135 and conjugated *H. influenzae* saccharide (see page 829, left-hand column, first full paragraph). Additionally the patients were administered multivalent pneumococcal polysaccharide compositions consisting of either conjugated or unconjugated forms of the saccharides. The document reports on the immune response to Hib,

MenA and several pneumococcal serotypes (see page 828, "Design" and "Conclusion", as well as Table 3).

12. Thus, document D7 discloses a composition comprising both Hib saccharide conjugate and unconjugated MenACYW135 saccharides. This is not disputed by the appellant.
13. The board holds that document D7 constitutes an appropriate starting point for the assessment of inventive step since it addresses immunisation against both *H. influenzae* and *N. meningitidis*, which is also the purpose of the claimed compositions.
14. The appellant has not argued that this document belongs to a different technical field, but quite to the contrary acknowledged that all the prior-art documents referred to in the present case belong to the same technical field as the invention (see point 3.12 of the statement of grounds of appeal).  
  
Instead, the appellant argued that the document was not directed to the same "*purpose and effect*" as the claimed invention. In particular, the document did not demonstrate the effect of the invention, namely a bactericidal response against MenW135, whereas both document D13 and document D6 did (see points 3.9 and 3.11 of the statement of grounds of appeal). One of these documents should therefore be considered to represent the closest prior art.
15. However, in the board's judgement, whether other documents constitute a more promising starting point is immaterial in the present case since the board holds that the claimed invention is obvious when starting from the disclosure in document D7.

As stated in decision T 967/97 (see point 3.2 of the Reasons, in particular the last paragraph), if inventive step is denied starting from a particular document as the closest prior art, the choice of starting point needs no specific justification.

Furthermore, a line of argument which leads to the finding of lack of inventive step cannot be successfully rebutted merely by submitting that there is closer prior art (see, for example, decision T 1742/12, point 10.3 of the Reasons).

16. In view of the above, further arguments by the appellant on the proper selection of the closest prior art need not be refuted. This applies to the appellant's argument based on the relative publication dates of the documents as well as that based on the technical effect achieved by the claimed invention.

*Technical effect and objective technical problem*

17. The claimed compositions are distinguished from the composition disclosed in document D7 in that the meningococcal saccharides are present in conjugated form.
18. The opposition division held that this difference resulted in improved immunogenicity of the saccharides such that the objective technical problem addressed by the claimed compositions was that of *"improving the immunogenicity of the meningococcal saccharides in the vaccine of D7"* (see page 20 of the decision).
19. The appellant argued that the effects achieved by the invention had not been taken into account by the

opposition division when formulating the problem. On the one hand, in document D7 there was no disclosure of the bactericidal response against MenW135. On the other hand, the patent showed an improvement in such a response, as could be seen from comparing the compositions 2 and 3 in the tables on pages 26 and 27 of the patent (corresponding to pages 26 and 27 of the patent application). This improved response was present without there being significant interference with the immune responses to MenA, C and Y.

20. The board notes that the improvement put forward by the appellant relates to a comparison of MenACW135Y conjugate compositions in the presence and absence of Hib conjugate. It therefore does not relate to a comparison with the composition disclosed in document D7, which already includes a Hib conjugate.

It is, however, established case law of the boards of appeal that the nature of the comparison with the closest prior art must be such that it demonstrates that the technical effect has its origin in the feature distinguishing the claimed subject-matter from that prior art.

In the case at hand this feature is the conjugation of the MenA, C, Y and W135 saccharides. Since the comparison between compositions 2 and 3 in the patent and in the application, respectively, is not suitable for demonstrating an effect due to conjugation of the saccharides, it also cannot serve to demonstrate any effect of this distinguishing feature on the immune responses or on a lack of interference between the immune responses to the various saccharides.

21. As noted above, the opposition division held that the difference between the subject-matter under consideration here and the vaccine disclosed in document D7 resulted in an improved immunogenicity of the meningococcal saccharides. It came to this conclusion in the absence of comparative data. However, the board considers this effect of the difference to be plausible on the basis of the common general knowledge on the effective date, as disclosed in documents D9a, D10 and D11 for example, namely that conjugation of capsular saccharides of the meningitis-causing bacteria *N. meningitidis*, *H. influenzae type B* and *S. pneumoniae* increased their immunogenicity. The increase in immunogenicity by conjugation of the saccharides is attributed to the generation of helper T-cell responses and immunological memory (see for example document D10, below).

D9a, a textbook on vaccines, discloses that a multivalent pneumococcal conjugate vaccine including a MenC conjugated saccharide, as well as a multivalent meningococcal conjugate vaccine - MenACYW135 - were under development. The authors express the expectation that these vaccines will have a great impact on the control of meningitis (see paragraph spanning the two columns on page 980).

D10, a review on meningococcal conjugate vaccines, states that meningococcal conjugated vaccines present advantages over plain polysaccharide vaccines, especially in children and adolescents. It notes that conjugates of capsular saccharides of MenA, C, Y and W135 have been prepared similarly to conjugates of pneumococcal conjugate vaccines and those of Hib conjugate vaccines. Both the Hib conjugate vaccine and the MenC conjugate vaccine were successful in improving

immunogenicity (see abstract and page 858, first full paragraph). D10 further states: "*Protein-polysaccharide vaccines have the advantage over polysaccharide vaccines alone. They generate helper T-cell (Th1) responses and create immunological memory responses [...] In addition to improved immunogenicity, the conjugate vaccines have a dramatic herd immunity effect through decreased transmission and nasopharyngeal carriage as demonstrated with Hib and conjugate pneumococcal vaccines [...] Mucosal immune response to a conjugate meningococcal C vaccine, measured by increased salivary IgG levels [...] is improved in both adult and child vaccines compared to those receiving the polysaccharide A/C vaccine*" (see page 858, first full paragraph).

D11, a review on therapies and vaccines for bacterial meningitis, highlights the introduction of conjugate vaccines as a major contribution to the control of meningitis caused by Hib and the expectation that it will lead to further improvements with regard to pneumococcal and meningococcal infection. In particular, a conjugate MenC vaccine had become available and a quadrivalent conjugate MenACW135Y vaccine was under development (see "*Introduction*", two last sentences and page 1055, last paragraph). According to this document, "*[t]he major advances in prevention of bacterial meningitis have come from conjugate vaccine technology [...] New vaccines are being licensed for meningococci and pneumococci, which are likely to have similar efficacy to that which has been seen with Hib vaccine*" (see page 1056, right-hand column, second full paragraph).

22. Thus, the board considers the objective technical problem to be the provision of a composition for

immunisation against infection by *N. meningitidis* and *H. influenzae* with improved immunogenicity.

*Obviousness*

23. The opposition division reasoned that the conjugation of the saccharides in order to solve the problem would have been obvious because advantages of conjugation were well known. Each of documents D10 and D13 were referred to in this respect.
24. Document D13 is concerned with meningococcal vaccines conferring broad protection against *N. meningitidis* infection, against a background of either monovalent, conjugated MenC saccharide or multivalent, unconjugated polysaccharide vaccines which were, however, not providing a satisfactory immune response. With this aim, document D13 provides all the saccharides individually conjugated to a carrier protein (see abstract and paragraphs 10, 11 and 15). In particular this document discloses a clinical trial with a tetravalent conjugate vaccine - MenACW135Y - using diphtheria toxoid as the carrier for all capsular saccharides (see examples 6 and 9).
25. In the board's judgement, the skilled person seeking to provide a composition with improved immunogenicity would have modified the composition disclosed in document D7 by providing the meningococcal saccharides in conjugate form as disclosed in document D13, i.e. conjugation of all of the meningococcal polysaccharides to diphtheria toxin, in order to achieve the advantages disclosed in that document.

26. The appellant submitted that the skilled person would have had no reason to expect that such a composition would result in an improved bactericidal immune response against W135 serogroup, good bactericidal immune responses against serogroup A, C and Y, and without significant immune interference. In other words, the appellant argued that the skilled person would not have expected to provide the effects listed by the appellant. However, these differential effects are not those which the skilled person had set out to achieve in accordance with the objective technical problem formulated above, i.e. the provision of a composition for immunisation against infection by *N. meningitidis* and *H. influenzae* with improved immunogenicity. Hence, the appellant's argument is not relevant in relation to the problem as formulated.
27. The appellant further argued that, although the skilled person was aware of the advantages of conjugation from documents D10 and D13, they were also aware of the problem of immune interference and would have been concerned that providing different conjugates in one single composition would affect the immune response to individual conjugates.
28. The board is not persuaded by this argument. The evidence before the board does not support the view that the skilled person would have expected interference when combining meningococcal and Hib conjugates, as argued by the appellant. Such concerns in particular are not supported by document D2, as submitted by the appellant, for the reasons below.

The appellant referred to the passage on page 1, lines 7 to 11, of document D2. The passage in question states that the development of multivalent vaccines is



complicated by the competition or interference between antigens. This generic and very brief statement does not mention conjugation at all. Moreover, the awareness of competition or interference did not deter the authors of the document from providing multivalent compositions, including compositions comprising Hib and meningococcal antigens, all individually conjugated to a carrier protein. In fact, the document discloses that combining the Hib antigens with antigens from other meningitis-causing agents led to an increase in the immunisation against Hib. In a clinical trial, a composition comprising Hib and MenAC conjugates was tested and the authors concluded that a good immune response against each antigen was observed (see example 3). More complex combinations were also tested, including, in addition to the above antigens, tetanus toxoid, diphtheria toxoid and a whole-cell pertussis component. A good immune response was observed here too (see example 3). Thus, reference to this document does not support the appellant's argument.

Document D5 also discloses combinations of Hib saccharide conjugates and meningococcal saccharide conjugates. It discloses kits comprising two or more separate vaccines, one of the vaccines being a composition comprising both a Hib conjugate and MenC and/or MenY conjugate (see page 5, lines 1 to 8). No teaching can be inferred from this document either which would have deterred the skilled person from combining a Hib saccharide conjugate with meningococcal saccharide conjugates.

29. Thus, the composition as claimed does not involve an inventive step, contrary to the requirements of Article 56 EPC.

*Auxiliary request 4*

30. Claim 1 of auxiliary request 4 differs from the embodiment considered in relation to claim 1 of the main request and of auxiliary requests 1 to 3 and 5 to 8 in that all meningococcal serogroup saccharides are conjugated to the CRM197 diphtheria toxin-mutant and that the composition comprises  $\leq 30 \mu\text{g}$  meningococcal saccharide per dose.
31. For the reasons given in points 13. to 15. above, the board considers document D7 to be a suitable starting point for the assessment of inventive step for this subject-matter too.
32. The appellant has not referred to any technical effects in addition to those achieved by the composition as defined in claim 1 of auxiliary request 1, and an additional technical effect was not apparent to the board. Thus, the objective technical problem remains the same as formulated above, namely the provision of a composition for immunisation against infection by *N. meningitidis* and *H. influenzae* with improved immunogenicity.
33. With regard to claim 1 of auxiliary request 4 the appellant submitted - as for claim 1 of auxiliary request 1 - that none of the cited documents specifically suggested the combination of features and that the skilled person would not have had a reasonable expectation that a composition with these features would achieve an improved bactericidal immune response against W135 without significant immune interference.

This argument has not been found to be persuasive in relation to claim 1 of the auxiliary request 1 (see point 29. above). The two additional features by means of which the claimed composition is defined do not change the board's assessment of the argument.

34. The appellant has not argued that the amount of saccharide or the choice of carrier would not lie within the possibilities known to the skilled person. The same applies to the provision of all conjugates with the same carrier protein.
35. Nevertheless, the board refers to prior-art document D13, which provides all four saccharides conjugated to diphtheria toxin. It thus discloses the use of the same carrier protein for all conjugates.

The carrier protein in the composition as defined in claim 1 is a mutant of diphtheria toxin, namely CRM197. This is, however, one of the possibilities that is well known to the skilled person, as demonstrated by the list on paragraph 27 of document D13.

Thus, in the board's judgement, when faced with the problem above, the skilled person would have provided the meningococcal saccharides all conjugated to the same carrier, the carrier being either diphtheria toxin as used in the examples in document D13 or an alternative carrier chosen from those listed as equivalent alternatives in this document.

36. The composition defined in claim 1 further specifies the amount of meningococcal saccharide to be at most 30 µg in the composition.

However, the tetravalent conjugate vaccine exemplified in document D13 contains 4 µg of each meningococcal saccharide, resulting in a total of 16 µg of saccharide (paragraph 78). Thus, the range of amounts specified in the claim is within what the skilled person would have provided without exercising inventive skill.

37. In view of the above considerations, the subject-matter of claim 1 is obvious in view of the combined teachings of documents D7 and D13 and hence does not fulfil the requirements of Article 56 EPC.

## Order

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chair:



I. Aperribay

G. Alt

Decision electronically authenticated