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Datasheet for the decision of 14 November 2013

Case Number: T 2134/10 - 3.3.08

Application Number: 97946850.1

Publication Number: 942983

IPC: C12N15/31, C07K14/315, G01N33/569, G01N33/68

Language of the proceedings: EN

Title of invention:
STREPTOCOCCUS PNEUMONIAE ANTIGENS AND VACCINES

Patent Proprietor:
HUMAN GENOME SCIENCES, INC.

Opponent:
Sanofi Pasteur Limited

Headword:
S. pneumoniae antigen/HUMAN GENOME SCIENCES

Relevant legal provisions:
EPC Art. 123(2), 84, 54, 56, 57
RPBA Art. 13(1)

Keyword:
Main Request: requirements of the EPC met (yes)

Decisions cited:
T 0939/92, T 1046/96, T 1170/02, T 1329/04, T 0898/05, T 0294/07, T 1511/07, T 0775/08, T 0018/09

Catchword:

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Case Number: T 2134/10 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 14 November 2013

Appellant: (Opponent)	Sanofi Pasteur Limited 1755 Steeles Avenue Toronto, Ontario M2R 3T4 (CA)
Representative:	Bizley, Richard Edward avidity IP Kestrel House Falconry Court Baker's Lane Epping, Essex CM16 5DQ (GB)
Respondent: (Patent Proprietor)	HUMAN GENOME SCIENCES, INC. 14200 Shady Grove Road Rockville, MD 20850 (US)
Representative:	Jaenichen, Hans-Rainer Vossius & Partner Siebertstrasse 4 81675 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 4 August 2010 concerning maintenance of the European Patent No. 942983 in amended form.**

Composition of the Board:

Chairman: M. Wieser
Members: B. Stolz
D. Rogers

Summary of Facts and Submissions

I. The appeal lies against the decision of the opposition division to maintain European patent No. 942983 in amended form on the basis of the main request filed during oral proceedings held on 21 May 2010.

II. With its statement setting out the grounds for appeal, the opponent (appellant) submitted a new document, D26.

III. With is reply, the patent proprietor (respondent) submitted new documents D27 to D32, and auxiliary requests 1 to 8.

IV. In a communication annexed to the summons to oral proceedings, the board informed the parties of its preliminary, non-binding opinion on some of the issues to be discussed at the upcoming oral proceedings.

V. With its final submissions, dated 14 October 2013, the respondent filed new documents D33 to D38, and auxiliary requests 9 to 38.

VI. With its final submissions, dated 22 October 2013, the appellant informed the board that it would not attend the oral proceedings.

VII. The appellant having previously announced its intention not to attend the oral proceedings, oral proceedings were held on 14 November 2013 with only the respondent being present. In the course of the proceedings, the respondent submitted a "New Main Request" and amended pages 2 to 20 of the description.

VIII. Independent claim 1 of the "New Main Request" reads as follows:

"1. A polynucleotide selected from the group consisting of
(a) polynucleotides encoding the polypeptide having the deduced amino acid sequence as shown in SEQ ID NO:66;

(b) polynucleotides having the coding sequence as shown in SEQ ID NO:65 encoding the polypeptide;

(c) polynucleotides which are at least 95% identical to the coding sequence as shown in SEQ ID NO:65;

(d) polynucleotides encoding a polypeptide having an amino acid sequence at least 95% identical to the amino acid sequence shown in SEQ ID NO:66;

(e) polynucleotides encoding an epitope-bearing portion of a polypeptide which comprises an amino acid sequence selected from the group consisting of:
Ile-486 to Ala-497; Asp-524 to Ala-535; His-662 to Gly-674 of the deduced amino acid sequence as shown in SEQ ID NO: 66; and

(f) polynucleotides encoding fragments comprising at least 50 contiguous amino acids of a polypeptide encoded by a polynucleotide of (a) or (b), wherein said fragments bear an antigenic epitope;

or the complementary strand of such a polynucleotide."

Claims 2 to 22 refer to the protein encoded by the polynucleotide of claim 1, vectors and host cells comprising the nucleic acid of claim 1, and to methods

and uses of the claimed nucleic acid and/or protein for diagnostic purposes.

IX. The following documents are cited in this decision:

D1: WO 96/08582

D6: Pearce B.J., et al., Molecular Microbiol. (1993) Vol. 9(5), 1037-1050

D8: Comparisons of SEQ ID NO: 65 of the Opposed Patent and SEQ ID NO: 34 of Dl

D15: Hamel J. et al. (2004) Infection and Immunity, 2659-2670

D17: WO 00/39299

D18: EP 0786 519 (HGS): front cover of A2 publication, description, claims and Table 4 as filed

D19: Alonso De Valesco E. et al. (1995) Microbiological Reviews, 591- 603

D21: Press release of Human Genome Sciences, Inc., dated 14th March 1996

D22: Paton J.C. et al., Microbial Drug Resistance, Spring 1997, Vol. 3(1), 1-10

D26: Alignment of BVH-11 fragments from documents D15 and D17 with Seq ID NO: 66

D36: Sutcliffe I.C. and Russell R.R.B., J. Bacteriol. (1995) 177(5), 1123- 1128

D37: Wizeman T.M. et al., Infect. Immun. (2001), 69(3), 1593-1598

D38: Seiberling M. et al., Vaccine (2012), 7455-7460

Exhibit A of respondent's submissions of 5 Mai 2008: Adamou et al., Infection and Immunity 69 (2001), 949-958

Exhibit D of respondent's submissions of 5 Mai 2008: Sequence comparison between the amino acid sequence shown in SEQ ID NO: 66 and the amino acid sequences of PhtD and PhtB of Annex A

X. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:

Article 123(2) EPC

According to the explanation to Table 1, the patent application originally filed merely provided 113 open reading frames (ORFs) encoding potentially antigenic peptides of S. pneumoniae. The granted patent focused on the protein defined by Seq ID NO: 66. By focusing the claims on one particular molecule, the patent proprietor gained an unwarranted advantage because from the application as originally filed it could not be derived which of the 113 molecules indeed had vaccine utility. More specifically added matter was present in claims 1(d), 1(e) and 1(f). In each case, the combination of the molecule defined by SEQ ID NOs: 65 and 66 with the specific features of these points of claim 1 were the result of a combination of features from two independent list of features, one list represented by Table 1 and the other lists taken from pages 3 to 5, and 25, respectively.

Only the publication by Adamou et al. (filed as Annex A with the patentee's submission of 5 May 2008) allowed the then applicant to focus its claims on Seq ID Nos: 65 and 66. This amounted to a classic "further element based on later findings" as referred to in paragraph 4 of the Reasons for the Decision in decision T 1046/96 of 19 January 1998. The Board was therefore asked to refer the following questions to the Enlarged Board of Appeal:

"1. If an applicant discloses in its originally filed application a large number of embodiments without establishing utility or indicating a particular preference for any such embodiment individually, in circumstances where the skilled person would not implicitly and automatically understand such established utility or particular preference, does the limitation of the claims to one embodiment during prosecution subsequent to relevant technical information provided by a third party constitute addition of matter contrary to Article 123(2) EPC?

2. Can the mere choice of subject matter from a single list ever constitute addition of matter, contrary to Article 123(2) EPC?

3. If the answer to question 2 is "yes", under what circumstances?"

Article 84 EPC

The addition of the feature "wherein said fragments bear an antigenic epitope" to claim 1(f) during opposition proceedings resulted in a clarity issue. Due to the use of the term "comprising" in "fragments

comprising at least 50 contiguous amino acids", said fragments could comprise further sequence elements not derived from Seq ID NO: 66 but still comprising undefined antigenic epitopes. The scope of protection of claim 1(f) was thus unclear.

Article 54 EPC

Document D1 disclosed Seq ID NO: 34, the reverse complement of which encoded a protein of 65 amino acids as shown in document D8. This sequence, albeit apart from a single amino acid change, corresponded to amino acids 668 to 732 of Seq ID NO: 66. In view of the ambiguous wording of claim 1(f) it fell within its scope.

Article 56 EPC

The claimed subject matter was obvious in view of the patent proprietor's public announcement that it was going to sequence the genome of S. pneumoniae (document D21) it was furthermore obvious because the sequencing of microbial genomes was routinely achievable and would have inevitably yielded Seq ID NOs: 65 and 66. It would also have been obvious to screen new ORFs for the presence of signal sequences and the LXXC lipoprotein motif as indicators of expression at the bacterial surface. Documents D6, D18 and D22 provided further evidence that the screening for surface accessible and/or exported proteins were well known in the art.

Claim 1 as maintained by the opposition division encompassed molecules which according to documents D15 and D17 were not providing protection against S. pneumoniae. According to the principles developed in decision T 939/92 (OJ EPO 1996, 309), the problem to be

solved could then not be formulated as the provision of a vaccine but only as the provision of means for diagnosing S. pneumoniae infection. The claimed solution was obvious starting from document D1 as closest prior art in combination with document D21, announcing the intention of the patent proprietor to sequence the entire genome of S. pneumoniae. Within the genome of S. pneumoniae, the skilled person would inevitably have found Seq ID NOs: 65 and 66. The sequences represented merely an arbitrary selection from the many possible solutions.

Article 57 EPC

The claims covered molecules unsuitable for protection against infection with S. pneumoniae. Should the board conclude that the claims related to S. pneumoniae antigens for the prevention or attenuation of disease, the claims lacked industrial applicability to the extent that the claims covered non-working embodiments.

XI. The arguments of the respondent, as far as relevant for the present decision, can be summarised as follows:

Article 123(2) EPC

The selection of the polypeptide of Seq ID NO: 66 did not constitute addition of new matter. Regarding the objections against claims 1(d), 1(e) and 1(f), the application disclosed the features referred to in these claims in relation to any of the polypeptides disclosed in table 1. This was clear from the paragraphs on page 4, lines 6 to 13, Table 2 and page 13, lines 21 to 24.

Article 84 EPC

The wording of claim 1(f) was clear and left no room for the interpretation that the epitopes were present within any, potentially added, protein portions.

Article 54 EPC

The nucleotide sequence disclosed in document D1 did not encode an amino acid sequence comprising 50 contiguous amino acids of Seq ID NO: 66.

Article 56 EPC

Documents D19 or D22 could be regarded as the closest prior art documents. The problem to be solved consisted in providing an alternative candidate molecule for improved vaccination against and diagnosis of S. Pneumoniae. This problem was solved by the the subject-matter of claim 1. Evidence for this could be found in documents D15 and D17. The N-terminal cysteine residue of the molecule of Seq ID NO: 66 rendered it plausible that the protein was attached to the cell membrane via this cysteine residue. Further evidence in this respect could be found in document D36. The patent itself contained no information that could contradict this conclusion. Hence the claimed molecule plausibly solved the technical problem, in line with the boards' case law as developed in decisions T 1329/04 of 28 June 2005, T 898/05 of 7 July 2006 and T 18/09 of 21 October 2009. As shown in documents D15, D17, Adamou et al., submitted as Annex A to the submissions of 5 May 2008, by Annex D to the submissions of 5 May 2008, and by document D38, the molecule of Seq ID NO: 66 belonged to a family of closely related surface exposed proteins of S. pneumoniae capable of protecting mice against infection. None of the cited prior art rendered it

obvious that the claimed molecule could be used to provide protection against several different serotypes.

Article 57 EPC

The technical problem of providing an alternative vaccine candidate was plausibly solved. Therefore, considering the criteria for assessing patentability as defined in decisions T 898/05 and T 18/09, the claimed solution was industrially applicable.

XII. The appellant requested in writing that the decision under appeal be set aside and that the patent be revoked. The appellant also requested to submit questions to the Enlarged Board of Appeal.

XIII. The final request of the respondent was that the decision under appeal be set aside and that the patent be maintained on the basis of claims 1 - 22 of the "New Main Request" and the description adapted thereto, both filed at the oral proceedings before the Board.

Reasons for the Decision

Admissibility of the "New Main Request"

1. The request filed at the oral proceedings before the board differs from the main request upheld by the opposition division and filed with the grounds of appeal by the deletion of certain epitopes in claim 1(e), the deletion of claims relating to the production of certain epitope bearing polypeptides, and the deletion of claims relating to vaccines and uses of the claimed peptides for vaccination purposes.

The deletion of several claims from the main request filed with the grounds of appeal neither creates a fresh case nor delays the procedure in any other way.

Therefore, the board, exercising its discretion under Article 13(1) RPBA, decided to admit the new main request filed at the oral proceedings.

Admissibility of documents D36 to D38

2. Documents D36 to D38 were filed in response to an objection raised by the board in the Annex to the summons to oral proceedings and were therefore admitted into the proceedings.

Article 123(2) EPC

3. The appellant objected that the limitation of the claimed subject matter to a single nucleic acid sequence (Seq ID NO: 65) and the corresponding amino acid sequence (Seq ID NO: 66), both selected from a list originally comprising 113 nucleic acid and amino acid sequences, respectively, contravened the requirements of Article 123(2) EPC.

4. The internationally published patent application WO 98/18930 relates to "Streptococcus pneumoniae antigens for the detection of Streptococcus and for the prevention or attenuation of disease caused by Streptococcus" (page 1, lines 1 to 3). It provides a Table 1, listing 113 polynucleotides from Streptococcus pneumoniae and the polypeptides encoded by these. The description of the invention refers *inter alia* to (emphasis added by the board):

"(a) a nucleotide sequence encoding **any of** the amino acid sequences of the polypeptides shown **in Table 1**; and (b) a nucleotide sequence complementary to **any of** the nucleotide sequences in **(a)**" (page 3, lines 21-22),

"isolated nucleic acid molecules that comprise a polynucleotide having a nucleotide sequence at least 90% identical, and more preferably at least 95% ....99% identical to **any of** the nucleotide sequences in **(a) or (b)**" (page 3, lines 24 to 28),

"isolated polypeptides having the amino acid sequences described in Table 1" (page 21, lines 24 to 25),

"antibodies elicited in an animal by the administration of **one** or more S. pneumoniae polypeptides **of the present** invention" (page 5, lines 14 to 16),

diagnostic methods relating to "assaying polypeptide levels using antibodies elicited in response to amino acid sequences described **in Table 1**" or to the use of nucleic acid probes "having all or part of a nucleotide sequence described in **Table 1**" (page 5, lines 20 to 23, and lines 28 to 30).

5. In each case, reference is made to the nucleic acid or amino acid sequences disclosed in Table 1. Table 1 consists of a single list of nucleic and amino acid sequences, among them the nucleic acid sequence of Seq ID NO:65 and the amino acid sequence of Seq ID NO: 66. The limitation to a single item from a single list of items, in the present case the limitation to subject matter related to Seq ID NOs: 65 and 66 only, is directly and unambiguously derivable from the application documents as filed.

6. This reasoning is consistent with the case law relating to Article 123(2) EPC, according to which the boards of appeal, in order to determine whether an amendment does or does not extend beyond the content of the application as filed, have to examine whether the amendment results in the introduction in the specification of information which the skilled person could not derive directly and unambiguously from that originally presented, when account is taken of matter which is implicit to a person skilled in the art in what has been expressly mentioned (cf. e.g. point 3 of the Reasons of decision T 1046/96 of 19 January 1998 and the decisions cited therein).

7. In view of the consistency of the instant decision with earlier decisions, the board cannot identify a reason that would justify the referral of the questions proposed by the appellant (cf. item X above) to the Enlarged Board of Appeal according to Article 112(1) EPC.

8. The appellant raised further specific objections under Article 123(2) EPC against parts (d), (e), and (f) of claim 1.

9. The subject matter of claim 1(d) is a polynucleotide encoding a polypeptide having an amino acid sequence at least 95% identical to the sequence shown in Seq ID NO: 66.

10. The appellant submitted that this embodiment of the invention resulted from the combination of items from two lists of features, which combination could not be derived from the application documents as filed.

11. The relevant paragraph on page 4 of the application documents as filed reads: "The polypeptides of the present invention also include polypeptides having an amino acid sequence with at least 70% similarity, and mor preferably at least 75% ..., 95%, ... similarity to those described in Table 1, as well as polypeptides having an amino acid sequence at least 70% identical, ... and still more preferably 80% ... 95%, ...identical to those above; as well as isolated nucleic acid molecules encoding such polypeptides."

Thus, there is direct and unambiguous disclosure of amino acid sequences displaying a specified degree of identity with each one of those displayed in Table 1, and to nucleic acids encoding such polypeptides. The restriction to amino acid sequences having at least 95% identity with Seq ID NO: 66 is then the result of a limitation to one specific degree of identity from among all the degrees specified on page 4. Contrary to appellant's submissions, there is no combination of independent features from two lists. A specific degree of sequence identity is not a property that, in combination with a particular molecule selected from Table 1, could single out a particular molecule or confer properties to the claimed subject matter not directly and unambiguously derivable from the application as filed.

12. The subject matter of claim 1(e) is a polynucleotide encoding an epitope bearing portion of a polypeptide which comprises one of three specifically mentioned peptide sequences defined by reference to Seq ID NO: 66.

13. The appellant submitted that the selection of epitopes from the list of epitopes presented in Table 2 in

combination with the selection of Seq ID NO: 66 from Table 1 was impermissible.

14. The patent application refers to "nucleotide sequences encoding epitope bearing portions of the S. pneumoniae polypeptides identified in table 1" as nucleic acid sequences of the present invention (page 13, lines 21 to 28). Table 2, page 98, under "SP042" (the designation given on page 66 of table 1 to Seq ID NO: 66), discloses a single list of epitope bearing polypeptides in individualized form derived from the protein of Seq ID NO: 66. Since the peptides are unambiguously disclosed as derived from Seq ID NO: 66, the board cannot follow appellant's argument that claim 1(e) represents an unallowable combination of features from a list of proteins and from a list of peptide fragments.

15. The subject matter of claim 1(f) is a group of polynucleotides encoding fragments comprising at least 50 contiguous amino acids of a polypeptide encoded by a polynucleotide of (a) or (b) (cf. point 3, above), wherein said fragments bear an antigenic epitope.

16. The appellant submitted that there was no disclosure of the term "contiguous" as such, of the feature "at least 50 contiguous amino acids" and of the combination of this feature with Seq ID NO: 66.

17. The paragraph mentioned in point 13, above, refers to nucleic acid molecules encoding epitope bearing portions of the polypeptides identified in Table 1. According to the paragraph bridging pages 24/25, the epitope bearing peptides and polypeptides, i.e. the antigenic epitope bearing fragments of the length specified on page 25, are contained within the amino

acid sequence of a polypeptide of the invention. This is a clear reference to nucleotides encoding peptides and polypeptides of the specified length comprising a contiguous portion of the protein of the invention. Thus, the board does not agree with the appellant's first objection.

18. According to the same paragraph, the length of the peptides is "at least seven, more preferably at least 9 and most preferably between 15 to about 30 amino acids" in length. "However, peptides ... comprising a larger portion ... containing about 30 to about 50 amino acids, or any length up to and including the entire amino acid sequence ... also are considered peptides or polypeptides of the invention ...".

While there is no explicit disclosure of the "at least 50 contiguous amino acids", there is explicit reference to short peptides, peptides of intermediate length (30 to 50 amino acids), and to peptides of any length up to the full length. The subrange of 30 to 50 amino acids lies clearly within the most generically defined range of "any length up to the full length". Contrary to the case in decision T 1511/07 of 31 July 2009, referred to by the appellant there is no combination of ranges belonging to different lists of features (cf. point 2.1 of the reasons of T 1511/07). The case at issue differs also from the case in decision T 1170/02 of 1 March 2006 where the numeric value of the upper limit of a range was taken from an example because it was only disclosed there (cf. point 4.5.1 of the Reasons). In the present case, both, the narrower range of 30 to 50 amino acids in length and the largest possible range were explicitly mentioned on page 25 and there is no need for extracting a value from an example. Under these circumstances, the range from 50 amino acids up

to the entire amino acid sequence of a polypeptide of the invention is directly and unambiguously derivable from the application as filed.

The combination of the particular range of polypeptide fragments with Seq ID NO: 66 is directly and unambiguously derivable from the reference in the paragraph bridging pages 24 and 25 to epitope bearing peptides of the invention, i.e. to those of Table 1.

19. The board is therefore satisfied that the requirements of Article 123(2) EPC are met.

Article 84 EPC

20. The appellant submitted that the wording of claim 1(f) was ambiguous because the newly added feature "wherein said fragments bear an antigenic epitope" left open whether the antigenic epitope had to be comprised within the at least 50 amino acids of a polypeptide according to parts (a) or (b) of claim 1, or whether they could be located in any other bit of sequence associated with but unrelated to the at least 50 amino acids encoded by a polynucleotide of (a) or (b).

21. The board cannot follow this argument. The term "fragments" in "fragments comprising at least 50 contiguous amino acids of a polypeptide encoded by a polynucleotide of (a) or (b)" can only refer to fragments of a polypeptide of 50 or more amino acids in length encoded by a polynucleotide of (a) or (b). Accordingly, said fragments bearing an antigenic epitope according to the second part of claim 1(f) can only bear antigenic epitopes from a polypeptide fragment encoded by a polynucleotide of (a) or (b).

22. The board is therefore satisfied that the requirements of Article 84 EPC are met.

Article 57 EPC

23. At the beginning of the appeal procedure, the appellant raised an objection of lack of industrial applicability, in case the board should find that the claims related to S. pneumoniae antigens for the prevention or attenuation of disease caused by S. pneumoniae. The reason being that claim 1(e) encompassed nucleic acid sequences which did not provide this functionality and hence lacked industrial applicability.

24. In the light of the actual set of claims and of the technical problem underlying the invention as defined in point (29) below, this objection is no longer of relevance.

Article 54 EPC

25. Document D1 discloses a nucleic acid sequence, Seq ID NO: 34, the reverse complement of which encodes a protein of 65 amino acids in length, as shown in document D8. The encoded protein almost matches amino acids 668 to 732 of SEQ ID NO: 66. As can be seen in document 8 and even stated in section G of appellant's grounds of appeal, there is a mismatch at the position corresponding to amino acid 697 in Seq ID NO: 66, leaving two matching fragments of 29 amino acids in the N-terminal portion and 30 amino acids in the C-terminal portion, respectively, encoded by the complementary sequence of Seq ID NO: 34. Neither this nucleic acid nor its complement encode a polypeptide comprising one of the epitopes according to claim 1(e). Nor do they

encode a polypeptide comprising at least 50 contiguous amino acids according to claim 1(f).

26. The board is therefore satisfied that the requirements of Article 54 EPC are met.

Article 56 EPC

27. Claim 1 refers to polynucleotides encoding a polypeptide defined by Seq ID NO: 66, closely related sequences and specific fragments thereof which are described as candidates for a vaccination against infection by S. pneumoniae (e.g. page 9, lines 6 to 8 of the published patent application).

28. Document D22 discusses several pneumococcal proteins and their role in the pathogenesis of pneumococcal infections, also in view of their potential as vaccine antigens. Document D19 reviews virulence factors of, and vaccines to prevent infection by S. pneumoniae. Contrary to document D22, the section on vaccines in document D19 focuses on polysaccharide protein conjugate vaccines. Therefore, document D22 is regarded as the closest prior art document.

29. Based on document D22, the problem to be solved is defined as the provision of an alternative candidate for vaccination against S. pneumoniae infection.

30. As a solution to this problem, the patent proposes the molecule as defined in claim 1.

31. However, the patent does not contain any experimental evidence regarding the properties of the claimed molecule.

32. The respondent has provided post published evidence in support of the alleged immune protective properties. Such evidence can however only be taken into account to back up information which is derivable from the patent itself (cf. e.g. point 10 of decision T 775/08 of 1 February 2011; point 8 of decision T 294/07 of 12 August 2010). It has therefore to be established whether the application makes it plausible that its teaching indeed solves the problem it purports to solve (cf. Headnote of decision T 1329/04 of 28 June 2005).

To test whether it is plausible that the problem has been solved in respect of Article 56 EPC, it first has to be decided whether the assignment of the claimed molecule to a defined group of molecules (in the present case the group of vaccine candidates) is correct. The board has then to consider whether additional information in the patent is in apparent contradiction with the claimed properties, and finally whether the group of molecules to which the claimed molecule is assigned share some properties that could reasonably be expected in the new molecule.

33. In opposition proceedings as well as in their written submissions in appeal proceedings, both parties considered the detection of an LPXTG or an LXXC motif in the ORFs of the isolated nucleic acid molecules as important for identifying surface exposed proteins, representing obvious candidates for vaccination. This is in line with the signature sequences said to have been used for the identification of the molecule defined by Seq ID NO: 66 (cf. page 10 of the published patent application).

Close inspection of Seq ID NO: 66 reveals however that it does not comprise any of the complete sequence motifs disclosed on page 10 of the patent application.

34. S. pneumoniae comprises lipoproteins tethered to the outer leaflet of its cell membrane via a lipid residue covalently linked to an N-terminal cysteine. When discussing the structural properties of pneumococcal surface adhesin A, the authors of document D22 noticed the presence of the consensus sequence LXXC at the carboxyl end of its N-terminal signal sequence, suggesting that the N-terminus of the protein was anchored via an N-acyl glyceride cysteine and thus closely associated with the cell membrane. This motif is the same motif as that mentioned, in its narrower form L-(A,S)-(G,A)-C, on page 10, lines 25 to 30 of the patent application. It was general knowledge, as exemplified by the minireview D36, that many lipoproteins of gram-positive bacteria possessed this consensus motif LXXC at the carboxy terminus of their signal sequence (cf. Table 1 of document D36), and that, after cleavage of the N-terminal signal sequence, the cysteine residue of this consensus motif became the N-terminal cysteine residue of the mature protein (cf. Table 2 of document D36).

35. According to page 9, lines 22 to 31, of the patent application, the polypeptides described have been modified to simplify the production of recombinant proteins. Nucleotide sequences encoding highly hydrophobic domains, such as those found at the amino terminal signal sequence have been excluded from some constructs. Furthermore, highly hydrophobic sequences at the carboxy terminus have also been excluded. Thus, the protein of Seq ID NO: 66 lacks its N-terminal signal sequence.

Notably, the first residue of Seq ID NO: 66 is a cysteine.

36. In view of the general knowledge about the role of an N-terminal cysteine in anchoring lipoproteins to the cell membrane, and the statement on page 9 of the patent application, that the N-terminal signal sequence of Seq ID NO:66 has been removed, the presence of the N-terminal cysteine in Seq ID NO: 66 serves as an indicator of anchorage of this protein to the cell membrane via a lipid residue.

In addition, post published Annex A, Adamou et al., shows that an LXXC motif is indeed present at the C-terminal end of the three closely related proteins phtA, phtB and phtD (cf. also points 39 and 40 below).

37. Since the patent contains no technical information that would contradict the potential attachment of Seq ID NO: 66 to the cell membrane, and since the skilled person would look for surface accessibility when looking for vaccine candidates (cf. e.g. page 31 of appellant's grounds of appeal), the board is satisfied that the claimed solution indeed solves the above mentioned technical problem.

38. It remains to be established whether the provision of the vaccine candidate according to claim 1 was obvious for a skilled person.

39. Post-published evidence submitted as Annex A with respondent's submissions of 5 Mai 2008 in opposition proceedings discloses a family of pneumococcal proteins that are protective against sepsis. The proteins designated as phtA, phtB and phtD were expressed in E.

coli and found to protect mice against pneumococcal infections.

An alignment of their sequences with the amino acid sequence of Seq ID NO: 66 has been provided as Annex D to respondent's submissions of 5 Mai 2008. While the protein of Seq ID NO: 66 lacks the N-terminal signal sequence and part of the C-terminal sequence, the comparison shows a considerable degree of sequence identity over its entire length in particular with the sequence of phtB (the total length of SEQ ID NO: 66 is 763 amino acids, with only 17 mismatches).

40. Based on the results from vaccination studies with fragments of phtB, published in documents D15 and D17 after the filing date of the patent at issue, the appellant submitted a chart, document D26, displaying an alignment of Seq ID NO:66 with the phtB (BVH11) sequence and emphasizing the positions of the predicted immunogenic epitopes. This chart shows, that several fragments of pthB (BVH-11B, NEW4, NEW5) comprising the same predicted epitopes as the protein of Seq ID NO:66 are immune protective.

Document D15 (Figure 7) discloses moreover that antibodies raised against phtB (BVH-11) recognise this protein in cell lysates from a broad selection of pneumococcal serotypes.

41. The appellant, referring to decision T 939/92 of 12 September 1995, has firstly argued that the claimed solution represented merely one of many equally obvious solutions and, secondly, encompassed several embodiments, in particular protein fragments comprising the N-terminal half of Seq ID NO:66 only, which were,

as shown by documents D15 and D17, unsuitable as vaccine candidates.

42. According to document D15, Figure 7, antibodies raised against the very closely related protein phtB detect this protein in 14 different serotypes of S. pneumoniae. Due to the close structural relationship between phtB and the protein of Seq ID NO:66, in particular the conservation of the predicted epitope sequences, the same can be reasonably expected of antibodies raised against the protein of the invention.

This property however, which is a generally desirable property of a vaccine candidate, but which, according to page 3, lines 11 to 12 of the of the patent application, in the case of S. pneumoniae vaccines has remained illusive until the present invention, sets the claimed molecule apart from the host of conceivably alternative solutions to the stated technical problem, rendering the claimed solution not an arbitrary solution in the sense of point 2.5.3. of decision T 939/92, but contributing to inventive step.

43. Regarding the second objection, claim 1 of the "New Main Request" refers only to epitope bearing portions of polypeptides comprising one of three epitopes specifically mentioned in claim 1(e). According to documents D15 and D17, fragments bearing these epitopes showed an immune protective effect (cf. appellant's summary of the results in document D26). As far as claim 1(f) is concerned, there is no evidence on file that any of the epitope bearing fragments would not be antigenic. Therefore, appellant's second objection is not relevant for claim 1 of the "New Main request".

44. In view of the above, the board decides that the "New Main Request" meets the requirements of Article 56 EPC.

45. At the oral proceedings, the respondent amended the description to bring it in line with the "New Main Request". The board is satisfied that this has been done in agreement with the requirements of the EPC.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the department of first instance with the order to maintain the patent as amended in the following version:

Description
Pages 21 - 25 of the patent specification as granted.
Pages 2 - 20 of the amended patent specification filed during the oral proceedings of 14 November 2013 before the Board.

Claims
Nos. 1 - 22 of the "New Main Request", filed during the oral proceedings of 14 November 2013 before the Board.

The Registrar: The Chairman:

A. Wolinski M. Wieser

Decision electronically authenticated