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Datasheet for the decision of 21 May 2015

Case Number: T 0895/13 - 3.3.04

Application Number: 06700004.2

Publication Number: 1835939

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Language of the proceedings: EN

Title of invention:
Meningococcal conjugate vaccination

Patent Proprietor:
Novartis AG

Opponents:

Headword:
Conjugates/NOVARTIS

Relevant legal provisions:
EPC Art. 83
EPC R. 115(2)
RPBA Art. 15(3)

Keyword:
All requests: sufficiency of disclosure (no)

Decisions cited:
G 0001/03, T 0609/02

Catchword:
see reasons, points 3 to 5

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Case Number: T 0895/13 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 21 May 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 5 February 2013 revoking European patent No. 1835939 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

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

Summary of Facts and Submissions

I. The appeal of the proprietor ("appellant") lies against the decision of the opposition division revoking European patent No. 1 835 939. The patent at issue has the title "Meningococcal conjugate vaccination".

II. The opposition division decided that the subject-matter of the main request then before it fulfilled the requirements of Article 83 EPC (see decision under appeal, points 2 to 5). It held (*ibid.*, point 2) that: "The patent does not actually provide an example of the subject-matter claimed. However, the patent discloses at least one way of executing the invention with CRM197 as carrier and the skilled person would have no difficulty in providing the composition with TT [tetanus toxoid, note by the board] as carrier." In the context of the assessment of inventive step (*ibid.*, points 3.4 and 4.7) the opposition division however held that: "no technical effect can be recognized for the subject-matter claimed". The subject-matter of the main request and of auxiliary requests 1 to 4 was found to lack an inventive step.

III. With its statement of grounds of appeal the appellant filed a main request and auxiliary requests 1 to 8.

The main request corresponds to auxiliary request 4 before the opposition division. Claim 1 reads:

"1. A composition that comprises at least two of: (a) a conjugate of (i) the capsular saccharide of serogroup A *N.meningitidis* and (ii) a tetanus toxoid; (b) a conjugate of (i) the capsular saccharide of serogroup C *N.meningitidis* and (ii) a tetanus toxoid; (c) a conjugate of (i) the capsular saccharide of serogroup

W135 *N.meningitidis* and (ii) a tetanus toxoid; and (d) a conjugate of (i) the capsular saccharide of serogroup Y *N.meningitidis* and (ii) a tetanus toxoid, for use in a method for immunising a human patient against a disease caused by *Neisseria meningitidis*, comprising the step of administering to the human patient the composition, wherein the patient has been pre-immunised within 1 year of the patient's birth with (a) a tetanus toxoid and/or (b) a conjugate of (i) a capsular saccharide of an organism other than *N.meningitidis* and (ii) a tetanus toxoid; and wherein the patient was pre-immunised at least six months before the method."

Claim 1 of auxiliary request 1 differs from claim 1 of the main request by requiring the composition to comprise all four of the conjugates (a), (b), (c) and (d), i.e. it must be a MenACWY conjugate.

Claim 1 of auxiliary request 2 corresponds to claim 1 of auxiliary request 1, but with the additional requirement that the composition contains no more than 50 µg of tetanus toxoid for all meningococcal conjugates combined.

Claim 1 of auxiliary request 3 corresponds to claim 1 of auxiliary request 2, but with the additional requirement that the conjugates are mixed to give a 1:1:1:1 ratio and each meningococcal antigen per dose is between 2 and 10 µg per serogroup.

Claim 1 of auxiliary request 4 corresponds to claim 1 of auxiliary request 3, but with the additional requirement that the patient has received tetanus toxoid as the T antigen in a D-T-P or D-T pre-immunisation.

Claim 1 of auxiliary requests 5 to 8 correspond to claim 1 of auxiliary requests 1 to 4, with the additional requirement that the meningococcal conjugates are administered as a single dose.

IV. Opponent 1 ("respondent") filed a response to the statement of grounds of appeal with letter of 31 October 2013.

V. A summons to oral proceedings was issued by the board and the parties were informed about the board's preliminary view in a communication pursuant to Article 15(1) RPBA. The board noted in its communication (see points 9 to 11), that the opposition division held (see decision under appeal, points 3.4 and 4.7) that no technical effect was provided in the patent for the subject-matter of claim 1 before it and that it did so in the context of assessment of inventive step. The board furthermore noted that, in view of point 2.5.2 of the reasons of decision G 1/03 and point 9 of the reasons of decision T 609/02, in the present case, the assessment of the technical effect provided by the claimed subject-matter was to be made in the context of the assessment of sufficiency of disclosure.

VI. With letter of 7 April 2015 the respondent withdrew its opposition. The respondent thus ceased to be a party to the appeal proceedings. The appeal proceedings were continued with the appellant as the sole party to the proceedings.

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

D21 Decker M.D. et al. chapter 29 in "Vaccines", 4th edition (2003), Plotkin S.A. and W.A. Orenstein editors, pages 825-861

D42 WO00/56360

D53 Marshall G.S. et al., The Pediatric Infectious Disease Journal (2010), vol. 29, pages 1-3

D54 Knuf M. et al., Vaccine (2011), vol. 29, pages 4264-4273

D55 Reddin K.M. et al., FEMS Immunology and Medical Microbiology (2001), vol. 31, pages 153-162

D56 WO02/00249

D57 AU748716B

VIII. Oral proceedings before the board were held on 21 May 2015. The appellant, although duly summoned was absent, as had been announced by letter of 7 May 2015. At the end of the oral proceedings the chairwoman announced the board's decision.

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

Sufficiency of disclosure (Article 83 EPC)

Main request: claim 1

The risk of carrier-suppression was well known at the priority date of the patent. The prior art suggested various approaches to avoid carrier suppression. Thus document D55 suggested the use of *Bordetella pertussis* fimbriae as a carrier protein instead of tetanus toxoid to reduce interference. Document D42 proposed the use of protein D to avoid carrier suppression. Document D56 proposed the use of a mixture of proteins as carriers for multiple conjugates. The prior art consistently taught that pre-immunisation with tetanus toxoid in particular could induce carrier suppression, see documents D42, D55, D56.

The patent however used tetanus toxoid antigen as the carrier for the meningococcal saccharides in claim 1.

The effect of the invention was the successful immunisation of patients that had been pre-immunised with tetanus toxoid with no signs of carrier suppression. This effect was recognised from the results in paragraph [0114] in the patent, and confirmed in many later documents like documents D53 and D54. The data summarised in paragraph [0114] and Table 1 showed that the vaccine induced a functional immune response. As noted in paragraph [0114], there was also no evidence of carrier suppression in these toddlers.

Auxiliary request 1: claim 1

The risk of the tetanus toxoid pre-immunisation causing carrier suppression for the MenACWY-tetanus conjugates was greater because of the greater number of conjugates.

Auxiliary requests 2 to 8

No further arguments were submitted in relation to these requests.

Note by the board: Although the appellant submitted the above arguments in the context of inventive step, the board took them into account in its assessment of sufficiency of disclosure (see section V above).

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

Sufficiency of disclosure (Article 83 EPC)

Main request: claim 1

Decision T 609/02 held (see point 9 of the reasons), that under Article 83 EPC, unless this was already known to the skilled person at the priority date, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application. In the present case, neither the patent nor the prior art disclosed the suitability of the product to be manufactured for the claimed therapeutic application including the dosage regimen. The trial exemplified in the patent only related to CRM197-conjugates.

Auxiliary request 1: claim 1

The disclosure was insufficient because neither the patent nor the prior art disclosed the suitability of the product to be manufactured for the claimed therapeutic application.

Auxiliary requests 2 to 8: claim 1

The amendments in these requests could not cure the insufficiency objected to with regard to the higher ranking requests.

XI. The appellant requested in writing that the decision under appeal be set aside and a patent be granted on the basis of the main request or on the basis of auxiliary requests 1 to 8, all filed with the statement of the grounds of appeal.

Reasons for the Decision

1. 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 the written submissions.

2. The invention concerns vaccines against *Neisseria meningitidis.* In particular, it concerns vaccines based on conjugated capsular saccharides from multiple meningococcal serogroups, specifically *Neisseria meningitidis* serogroups A, C, W125 and Z. The conjugates contain tetanus toxoid as the carrier

protein and are used for immunising patients that have been pre-immunised with tetanus toxoid at least 6 months previously.

Sufficiency of disclosure (Article 83 EPC)

Main request: claim 1

3. Claim 1 is a purpose-related product claim drawn up in accordance with Article 54(5) EPC and relates to a composition for use in a method for immunising a human patient against a disease caused by *Neisseria meningitidis* (see section III above for the complete wording of the claim).

4. In decision T 609/02 (see point 9 of the reasons) the board held that:

"Where a therapeutic application is claimed in the form allowed by the Enlarged Board of Appeal in its decision G 5/83 (OJ EPO 1985, 64), i.e. in the form of the use of a substance or composition for the manufacture of a medicament for a defined therapeutic application, attaining the claimed therapeutic effect is a functional technical feature of the claim (see G 2/88 and G 6/88, OJ EPO 1993, 93 and 114, Headnote III. and point 9 of the reasons, for non-medical applications, see also T 158/96 of 28 October 1998, point 3.1 of the reasons)."

5. Pursuant to decision T 609/02, attaining the claimed therapeutic effect is a functional technical feature of a claim drawn up in the Swiss type form. In the board's view, the same principle applies to purpose-related product claims drawn up in accordance with Article 54(5) EPC. Accordingly, in the present case, the

examination of the therapeutic effect provided by the claimed subject-matter is to be made in the context of the assessment of sufficiency of disclosure (Article 83 EPC), see decision G 1/03 (reasons, see point 2.5.2) and not in the context of the assessment of inventive step, as in the decision under appeal (see section II, above).

6. According to decision T 609/02 (*ibid.*):

"(...) under Article 83 EPC, unless this is already known to the skilled person at the priority date, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application."

7. In the present case, the product to be manufactured is a composition comprising at least two conjugates of a capsular saccharide of *N. meningitidis* and tetanus toxoid. The therapeutic application is the immunisation of a human patient against a disease caused by *Neisseria meningitidis,* wherein the patient has been pre-immunised with tetanus toxoid. Hence, the therapeutic effect to be achieved by the compounds referred to in the claims can be seen as the successful induction of an immune response against *Neisseria meningitidis* in a patient pre-immunised with tetanus toxoid.

8. For the assessment of the suitability of the compounds referred to in the claim to achieve the therapeutic effect, the teaching of the patent and the common general knowledge of the skilled person are to be taken into account. The decisive date for this assessment is the effective date of the claim. Post-published evidence may be taken into account, but only to back-up

the findings in the patent, and not to establish sufficiency of disclosure on its own (see decision T 609/02, *ibid.*).

9. At the priority date of the present patent the skilled person was aware of the phenomenon of "carrier suppression" which results in the inhibition of an immune response against an antigen conjugated to a particular carrier protein when the subject has already been pre-immunised with that carrier protein. In other words, the prior exposure to the carrier protein reduces the later immune response to an antigen conjugated to that carrier (see e.g. document D21, page 831, left hand column, third paragraph; and document D55, paragraph bridging left and right hand columns on page 160).

10. The prior art teaches also that pre-immunisation with tetanus toxoid in particular suppresses the immune response to later administered tetanus-toxoid based saccharide conjugates (see document D21, *ibid.*; document D42, page 7, lines 7 to 9; and document D55, *ibid.*).

11. It was also well established in the art at the priority date of the patent that the occurrence of carrier suppression is unpredictable and must be evaluated for each particular vaccine combination (see document D21, *ibid.*).

12. The prior art proposes a number of different approaches for avoiding carrier suppression in patients such as the use of more than one carrier (see document D56, page 3, lines 2 to 5; and document D57, page 4, lines

16 to 22) or of alternative carriers (see document D55, page 154, left hand column, second full paragraph).

13. In contrast, the present invention involves the use of the same type of carrier, tetanus toxoid (TT), for all of the two or more MenA, MenC, MenW and MenY conjugates, which carrier is the same antigen as has been used for pre-immunisation of the patients at least 6 months previously.

14. The patent shows (see paragraphs [0111] to [0114]), that a tetravalent vaccine based on a mixture of capsular saccharides of *N. meningitidis* conjugated to the carrier CRM197 - a detoxified mutant of diphtheria toxin - is immunogenic without any evidence of carrier suppression. Paragraph [0114] of the patent describes a clinical trial in which four different *N. meningitidis* MenACWY vaccines and a MenCWY vaccine were administered to between 12 and 16 months old toddlers. 25% of the patients received a further dose 4 weeks later. The data summarised in paragraph [0114] and in Table 1 show that the vaccine induced a functional immune response. As noted in paragraph [0114] there was also no evidence of carrier suppression in these toddlers.

15. However, as a matter of fact, the claimed vaccine which is based on tetanus toxoid as the carrier has not been exemplified in the patent. No data are reported in the patent for meningococcal conjugates using tetanus toxoid as the carrier.

16. In view of the well established phenomenon of carrier suppression, in particular in the context of tetanus toxoid (see point 10 above), and the known unpredictability of carrier suppression in the context of conjugate vaccines (see point 11 above), the results

obtained in the patent with CRM197 as the carrier do not make it plausible that meningococcal conjugates using tetanus toxoid as the carrier are suitable for the successful immunisation of patients that had been pre-immunised with tetanus toxoid.

17. Under these circumstances, post-published evidence cannot be taken into account for the establishment of sufficiency of disclosure (see point 8 above).

18. In view of the above considerations and in the light of decision T 609/02, the subject-matter of claim 1 of the main request fails to meet the requirements of Article 83 EPC and the request is therefore not allowable.

Auxiliary requests 1 to 8: claim 1

19. Since the subject-matter of claim 1 of auxiliary requests 1 to 8 concerns a composition for use in a method for immunising a human patient against a disease caused by *Neisseria meningitidis*, wherein the capsular polysaccharides of *Neisseria meningitidis* are conjugated to tetanus toxoid as the carrier, the board's conclusions under Article 83 EPC for the subject-matter of claim 1 of the main request (see points 1 to 17, above) apply, *mutatis mutandis,* to the subject-matter of claim 1 of auxiliary requests 1 to 8. These requests are therefore not allowable.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated