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**Datasheet for the decision
of 11 December 2018**

Case Number: T 2510/13 - 3.3.08

Application Number: 04804357.4

Publication Number: 1706481

IPC: C12N1/21

Language of the proceedings: EN

Title of invention:

VACCINE

Applicant:

GlaxoSmithKline Biologicals s.a.
Utrecht University

Headword:

Neisserial bacterium/GLAXOSMITHKLINE

Relevant legal provisions:

EPC Art. 84, 113(1)

Keyword:

Main request and auxiliary requests 1 to 8 - clarity (no)

Decisions cited:

G 0010/93

Catchword:



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Case Number: T 2510/13 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 11 December 2018

Appellants: GlaxoSmithKline Biologicals s.a.
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 18 July 2013
refusing European patent application No.
04804357.4 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman B. Stolz
Members: M. R. Vega Laso
D. Rogers

Summary of Facts and Submissions

- I. The appeal lies from a decision of an examining division under Article 97(2) EPC posted on 18 July 2013, refusing the European patent application No. 04804357 with the title "Vaccine". The application had been filed under the Patent Cooperation Treaty and published as WO 2005/064021.
- II. In the decision under appeal, the examining division found that the subject-matter of claims 8 to 12 and 14 to 19 of the main request lacked novelty. The same applied, *mutatis mutandis*, to the subject-matter of the corresponding claims in auxiliary requests 1 to 3 and 5. The claims according to auxiliary request 4 were considered not to meet the requirements of Article 84 EPC.
- III. Claims 1, 8 and 10 according to the **main request** read as follows:
- "1. A Neisserial bacterium in which the expression of Imp protein, the Imp amino acid sequence in strain MC58 being SEQ ID NO:21, the Imp amino acid sequence in strain FAM18 being SEQ ID NO:22 and the Imp amino acid sequence in strain Z2491 being SEQ ID NO:23, is functionally downregulated such that the level of LPS in the outer membrane is decreased compared to wild-type Neisserial bacterium by: downregulating expression from the *imp* gene, disrupting the *imp* gene so that no expression occurs, or disrupting the structure of the Imp protein.
8. An outer membrane vesicle preparation derived from the bacterium of any one of claims 1-7.

10. The outer membrane vesicle preparation of any one of claim 8 or 9 wherein the level of LPS is sufficiently low so that the toxicity is reduced to a level at which the outer membrane vesicle preparation has an acceptable level of reactogenicity when inoculated into a patient."

Dependent claims 2 to 7 are directed to various embodiments of the Neisserial bacterium of claim 1, and claims 9, 11 and 12 to embodiments of the outer membrane vesicle preparation of claim 8. Claims 14 to 17 relate to pharmaceutical compositions comprising the bacterium of claims 1 to 7 or the outer membrane vesicle preparation of any one of claims 8 to 12, and a pharmaceutically acceptable carrier. Claims 18 and 19 are directed to the outer membrane vesicle preparation, the pharmaceutical composition or the bacterium for use in the treatment of prevention of a Neisserial infection.

- IV. Claim 1 of the **auxiliary request 1** differs from claim 1 of the main request in that the Imp protein is further defined as "*... also being called OstA and encoded by the imp gene*". Claim 1 of the **auxiliary request 2** specifies as a further feature that the claimed Neisserial bacterium is "*isolated*".
- V. Claim 1 of the **auxiliary request 3** differs from the corresponding claim of the auxiliary request 1 in that it specifies that the expression of the imp gene is downregulated "*... such that the amount of Imp in the outer membrane is decreased by at least 60% ...*". The remaining claims 2 to 19 of auxiliary requests 1 to 3 are identical in wording to those of the main request.

VI. Claim 1 of the **auxiliary request 4** is directed to a method for producing a Neisserial bacterium with the same features specified in claim 1 of the main request. The method is characterized by the step of downregulating expression from the *imp* gene, disrupting the *imp* gene so that no expression occurs, or disrupting the structure of the Imp protein. Claims 8 and 10 read as follows:

"8. A method for producing an outer membrane vesicle preparation comprising the steps of: culturing the bacterium of claims 1-7, and producing an outer membrane vesicle preparation from said culture.

10. The method of any one of claim 8 or 9 wherein the level of LPS in the outer membrane vesicle is sufficiently low so that the toxicity is reduced to a level at which the outer membrane vesicle preparation has an acceptable level of reactogenicity when inoculated into a patient."

Claims 2 to 7 and claims 9, 11 and 12 are directed to various embodiments of the method of, respectively, claim 1 and claim 8. Claims 13 to 16 relate to a method for producing a pharmaceutical composition comprising the method of claims 1 to 7, or the method of claims 8 to 12.

VII. Claims 1 to 18 of the **auxiliary request 5** differ from the claims of the auxiliary request 1 in that the wording "... *downregulating expression from the imp gene, ...*" in claim 1, as well as the complete claim 2 have been deleted, and the remaining claims have been re-numbered and the dependencies amended accordingly.

- VIII. The applicants (appellants) filed an appeal against the refusal of the application. Together with their statement setting out the grounds of appeal, the appellants re-filed the sets of claims according to the main request and auxiliary requests 1 to 5 underlying the decision under appeal, and submitted three additional sets of claims as new auxiliary requests 6 to 8, and documentary evidence. As a subsidiary request, they requested oral proceedings.
- IX. The set of claims according to the **auxiliary request 6** corresponds essentially to the claims of the main request, except that the feature "*..., wherein the concentration of lipoproteins in the outer membrane vesicles is equivalent to the concentration of lipoproteins from outer membrane vesicles derived from a non-detergent extraction process*" has been inserted into claim 8, and claim 12 has been deleted.
- X. Claims 1 to 14 of the **auxiliary request 7** correspond to claims 1 to 7 and 13 to 19 of the main request. Since the claims directed to an outer membrane vesicle preparation (claims 8 to 12 of the main request) have been deleted in this request, also the references to the preparation in claims 9, 13 and 14 have been deleted.
- XI. Finally, the set of claims of the **auxiliary request 8** is identical to that of the auxiliary request 4 (see section VI above), except that claim 8 has been amended to read "*... culturing the bacterium made by the method of claims 1-7 ...*" (emphasis added by the board) and the dependency of claim 14 corrected.

- XII. The examining division did not rectify its decision and the case was remitted to the Board of Appeal (Article 109 EPC).
- XIII. The appellants were summoned to oral proceedings.
- XIV. In response to the summons, the appellants informed the board that they would not be represented at the oral proceedings.
- XV. In a communication sent to the appellants, the board provided some observations on issues relating to Articles 84 and 54 EPC, and expressed the provisional opinion that none of the sets of claims on file met the requirements of Article 84 EPC, and that therefore the appeal was likely to be dismissed.
- XVI. Oral proceedings were held on 11 December 2018 in the absence of the appellants.
- XVII. The appellants did not make any submissions on the issues relevant to this decision.
- XVIII. The appellants (applicants) requested in writing that the decision under appeal be set aside and that a patent be granted according to the main request, filed under cover of a letter dated 4 June 2013, or alternatively according to one of auxiliary requests 1 to 5, all filed under cover of a letter dated 3 July 2013, or alternatively according to one of auxiliary requests 6 to 8, all filed under cover of a letter dated 22 November 2013.

Reasons for the Decision

Main request - Article 84 EPC

1. In the decision under appeal, the examining division found that the claims according to the main request fulfilled the requirements of Article 84 EPC, but that their subject-matter lacked novelty. In line with decision G 10/93 of the Enlarged Board of Appeal (OJ EPO 1995, 172, see Order), in an appeal against a decision of an examining division the board is not limited to examine the issues on which the examining division decided adversely, but is empowered to decide whether the claims and the invention to which they relate fulfil the patentability requirements of the EPC, and to raise new objections if it considers it necessary.
2. In its communication in preparation of the oral proceedings, the board pointed to various deficiencies of the claims concerning Article 84 EPC. In particular, the board expressed the provisional opinion that the wording "*..., the Imp amino acid sequence in strain MC58 being SEQ ID NO:21, the Imp amino acid sequence in strain FAM18 being SEQ ID NO:22 and the Imp amino acid sequence in strain Z2491 being SEQ ID NO:23, ...*" in claim 1 was vague and left open whether the specified sequences of the Imp protein were a limiting feature of the claimed Neisserial bacterium.
3. Moreover, it was stated in the board's communication that, according to claim 1, the expression of Imp protein in the claimed Neisserial bacterium was functionally downregulated by, *inter alia*, downregulating expression of the *imp* gene, such that the level of LPS in the outer membrane was decreased

compared to wild-type Neisserial bacterium. However, claim 1 did not specify to which extent the expression of the *imp* gene is downregulated, and/or the level of LPS in the outer membrane is decreased. Therefore, the board was of the view that claim 1 did not define the Neisserial bacterium for which protection was sought in a clear manner.

4. In its communication, the board raised further issues under Article 84 EPC concerning claims 9, 10, 18 and 19. In particular, as regards claim 10 the board held that the terms "sufficiently low" and "acceptable level" characterizing, respectively, the level of LPS in the claimed outer membrane vesicle preparation and the level of reactogenicity when the preparation is inoculated into a patient, were indefinite.
5. The appellant neither remedied these deficiencies nor put forward any arguments that could persuade the board to revise its adverse provisional opinion concerning the compliance of the claims with Article 84 EPC.
6. Hence, for the reasons given above the claims according to the main request do not meet the requirements of Article 84 EPC.

Auxiliary requests 1 to 8 - Article 84 EPC

7. The findings on Article 84 EPC in connection with claim 1 of the main request (see paragraphs 2 and 3 above) apply equally to claim 1 of each of the auxiliary requests 1, 2, 5, 6, and 7.
8. Even if the board were to accept that the amendment introduced in claim 1 of the auxiliary request 3 (see section V above) remedies the clarity issue concerning

the extent to which the expression of the *imp* gene is downregulated and/or the level of LPS in the outer membrane is decreased, for the reason given in paragraph 2 above the claim still fails to define the matter for which protection is sought in a clear manner.

9. Claim 10 of the auxiliary requests 1, 2, 3 and 6, as well as claim 9 of the auxiliary request 5 suffer from the same clarity deficiency as claim 10 of the main request (see paragraph 4 above).
10. As regards auxiliary requests 4 and 8 (see sections IV and XI above), in which claims 1 and 10 have been reformulated as method claims, the findings in paragraphs 2 and 4 in connection with the main request also apply, *mutatis mutandis*.
11. Since none of the sets of claims on file meets the requirements of Article 84 EPC, a patent cannot be granted on the basis of any of the requests. Consequently, the appeal must be dismissed.

Article 113(1) - right to be heard

12. The grounds on which the present decision is based are known to the appellants as they were among those given for the board's provisional opinion expressed in the communication sent in preparation of the oral proceedings. Despite the board's provisional conclusion that none of the sets of claims on file met the requirements of Article 84 EPC (see point 26 of the board's communication), the appellants neither replied to the communication nor attended the oral proceedings.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



L. Malécot-Grob

B. Stolz

Decision electronically authenticated