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**Datasheet for the decision
of 29 November 2018**

Case Number: T 1547/15 - 3.3.03

Application Number: 04791697.8

Publication Number: 1678212

IPC: C08B37/00, A61K39/095,
A61K31/715

Language of the proceedings: EN

Title of invention:

HYPO- AND HYPER-ACETYLATED MENINGOCOCCAL CAPSULAR SACCHARIDES

Patent Proprietor:

GlaxoSmithKline Biologicals SA

Relevant legal provisions:

EPC Art. 56

Keyword:

Inventive step - (all requests: no)



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Case Number: T 1547/15 - 3.3.03

D E C I S I O N
of Technical Board of Appeal 3.3.03
of 29 November 2018

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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 26 May 2015
revoking European patent No. 1678212 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairman D. Semino
Members: O. Dury
R. Cramer

Summary of Facts and Submissions

- I. The appeal by the patent proprietor lies against the decision of the opposition division posted on 26 May 2015 revoking European patent No. 1 678 212.
- II. Two notices of opposition against the patent were filed.
- III. One of the oppositions was withdrawn with letter of 26 March 2015.
- IV. The contested decision was based on a main request (patent as granted) and on auxiliary requests 1 to 4, all filed with letter of 13 February 2015.

Claims 1 and 2 of the **main request**, read as follows:

"1. A modified serogroup W135 meningococcal capsular saccharide, conjugated to a carrier protein, wherein:
(a) between 2-9% of the sialic acid residues in the saccharide are O-acetylated at the 7 position; and/or
(b) between 35-55% of the sialic acid residues in the saccharide are O-acetylated at the 9 position."

"2. A modified serogroup Y meningococcal capsular saccharide, conjugated to a carrier protein, wherein
(a) between 2-9% of the sialic acid residues in the saccharide are O-acetylated at the 7 position; and/or
(b) between 35-55% of the sialic acid residues in the saccharide are O-acetylated at the 9 position."

Claims 1 and 2 of **auxiliary request 1** differed from claims 1 and 2, respectively, of the main request in that the expression "conjugated to a carrier protein" was replaced by "conjugated to CRM₁₉₇ carrier protein".

Claim 1 of **auxiliary request 2** was identical to claim 2 of the main request.

Claims 1 and 2 of **auxiliary request 3** differed from claims 1 and 2, respectively, of the main request in that the following expression was added at the end of the claims:

"and (c) the conjugate is obtainable by the introduction of an amino group into the saccharide followed by derivatisation with an adipic diester and reaction with the carrier protein".

Claims 1 and 2 of **auxiliary request 4** read as follows:

"1. A modified serogroup W135 meningococcal capsular saccharide, conjugated to a carrier protein, wherein between 2-9% of the sialic acid residues in the saccharide are O-acetylated at the 7 position."

"2. A modified serogroup Y meningococcal capsular saccharide, conjugated to a carrier protein, wherein between 2-9% of the sialic acid residues in the saccharide are O-acetylated at the 7 position."

V. The following documents were, *inter alia*, cited in the contested decision:

D1: WO 03/007985

D2: Jones and Lemercinier, J. Pharm. Biomed. Anal., 2002, 30, pages 1233-1247

D3: WO 02/091998

D5: Lemercinier and Jones, Carbohydr. Res., 1996, pages 83-96

D14: Longworth et al., FEMS Immunol. Med.

Microbiol., 2002, 32, pages 119-123

D20: Claus et al., Molecular Microbiology, 2004,
51(1), pages 227-239

D21: Pollard et al., Emerging Infectious Diseases,
2003, 9(11), pages 1503-1504

VI. In the contested decision, the opposition division held that the grounds of opposition under Article 100(c) EPC together with Article 123(2) EPC, Article 100(b) EPC and Article 100(a) EPC together with Article 54 EPC did not prejudice maintenance of the patent as granted but that of Article 100(a) EPC together with Article 56 EPC did. Also, none of auxiliary requests 1 to 4 was considered to satisfy the requirements of Article 56 EPC. The reasons given were, as far as relevant to the present decision, as follows:

(a) Regarding novelty of the main request over D1, the opposition division held that D1 disclosed a method for manufacturing certain oligosaccharides, which was virtually the same as the one of the patent in suit. It was further derivable from the information provided in D1 and in the patent in suit that the conjugates prepared in D1 were the same as the ones of the patent in suit. However, since D1 failed to indicate the bacteria used to manufacture the polysaccharides, the products of D1 were not made available to the public. Therefore, although D1 effectively disclosed a method according to which the conjugates could have been prepared, it failed to actually disclose conjugates as defined in granted claims 1 and 2. For these reasons, granted claims 1 and 2 were novel over D1 (section 3.3 of the decision).

- (b) Regarding inventive step of the main request, the analysis of the opposition division was as follows (section 3.4 of the decision):

Considering that the patent in suit dealt with the manufacture of meningococcal capsular saccharides conjugated to carrier proteins and the investigation of the immunogenicity of such conjugates, D1, in particular claim 1 thereof, was a suitable closest prior art document since it dealt with the manufacture of vaccines against meningococcal infections.

The subject-matter of granted claims 1 and 2 differed from said closest prior art in that it was characterised in terms of the specific levels of acetylation mentioned therein, whereas D1 was silent in that respect.

In the absence of any evidence that said distinguishing feature was related to a technical effect, the technical problem effectively solved by granted claims 1 and 2 resided in the provision of an alternative conjugate.

D1 disclosed how to manufacture potential vaccines, in particular employing meningococci of serogroups W135 and Y conjugated to a carrier protein. In order to provide a mere alternative to D1, it was obvious to use any polysaccharide. The opposition division then concluded "By choosing any polysaccharide, he (the skilled person) would thus also chose a polysaccharide which is almost identical to the one that has been specifically employed in the examples of the patent in suit. By doing so, there cannot be the shadow of a doubt

that he would then have arrived to the claimed subject-matter."

A similar analysis was valid for each of the pending auxiliary requests (sections 4.2 and 5 to 7 of the reasons of the decision).

VII. The patent proprietor (appellant) appealed the above decision. With the statement setting out the grounds of appeal the appellant requested that the opposition division's decision be set aside and that the opposition be rejected (main request) or, in the alternative, that the patent be maintained in amended form according to any of auxiliary requests 1 to 4 filed therewith. Each of the main request and of auxiliary requests 1 to 4 was identical to the main request and to auxiliary requests 1 to 4 dealt with in the contested decision, respectively. Also the following document was filed:

D24: Michon et al., Physico-Chemical Procedures for the Characterisation of Vaccines, Dev. Biol. Basel, Karger, 2000, 103, pages 151-160

VIII. Issues to be discussed at oral proceedings were specified by the Board in a communication. It was in particular indicated therein that it could have to be discussed whether D20 and D21 were valid prior art documents, whereby the burden of proof was on the party relying on those documents (see section 4.3).

IX. With letter of 22 August 2018 the appellant withdrew its request for oral proceedings but explicitly maintained the appeal. It was further requested that a decision be taken on the basis of the written

submissions.

- X. The second opposition was withdrawn with letter of 28 August 2018.
- XI. Oral proceedings were held on 29 November 2018 in the absence of the appellant, as announced.
- XII. The appellant's arguments, insofar as relevant to the decision, may be summarised as follows:

Main request - Inventive step

- (a) D3, and not D1, was the closest prior art document.
- (b) However, should D1 be held to constitute the closest prior art, the subject-matter of granted claims 1 and 2 differed therefrom in that the conjugates defined therein were acetylated and had to exhibit specific, narrow, levels of acetylation at either the 7 or the 9 position. In that respect, D1 contained no disclosure of any acetylation levels at any position in the final conjugates.
- (c) Figures 3 to 6 as well as paragraphs 170 to 172 of the patent in suit showed that the technical effect resulting from the above distinguishing feature was a better defined conjugate that induced an effective immune response, which meant that an effective vaccine could be reliably reproduced. The technical problem was therefore to provide improved Men W135 and Men Y conjugates that induced an effective immune response and were better defined.

- (d) The skilled person starting from D1 did not know which starting strains were used to make the conjugates or what the acetylation status of those conjugates was. Therefore, there was no reason why the skilled person aiming at providing improved Men W135/Men Y conjugates that induced an effective immune response and were better defined would have chosen an O-acetylation positive starting strain and conjugation conditions that resulted in the claimed O-acetylation patterns. In particular, considering that e.g. D2 taught that O-acetylation was not important for immunogenicity and that D24 taught that O-acetylation reduced immunogenicity, the skilled person would have been taught away from the subject-matter of granted claims 1 and 2.

Even if the problem solved resided in the mere provision of alternative conjugates, as held by the opposition division, the teaching of the prior art regarding the importance of the O-acetylation of Men W135 and Men Y conjugates was confused at the priority date of the patent in suit, some of those documents indicating explicitly that the O-acetylation was not important or was uncertain (see e.g. paragraphs 7-9 of the patent in suit as well as D2, D5, D14, D20, D21 and D24). Under those circumstances, there was no guidance in the prior art from which the skilled person could have reasonably predicted the O-acetylation pattern of Men W135 and Men Y conjugates, or whether conjugates having the claimed structure were immunogenic when used as vaccines.

- (e) In view of the above, the subject-matter of granted claims 1 and 2 was inventive.

Auxiliary requests 1 to 4

(f) Auxiliary requests 1 to 4 were inventive for the same reasons as outlined for the main request.

XIII. The appellant requested that the decision under appeal be set aside and the patent be maintained as granted (main request) or, in the alternative, that the patent be maintained in amended form according to any of auxiliary requests 1 to 4 filed with the statement of grounds of appeal.

Reasons for the Decision

1. Procedural issue

1.1 Both oppositions lodged against the patent in suit were withdrawn, either during the opposition proceedings or during the appeal proceedings (see sections III and X above). Since no request regarding apportionment of costs was made, the appellant is the sole party remaining to the current proceedings. According to established case law (Case Law of the Boards of Appeal of the EPO, 8th edition, 2016, IV.C.4.3.3) the withdrawal of an opposition has no direct procedural consequences for the appeal proceedings if the opponent was the respondent and the patent was revoked by the contested decision (i.e. as in the present case), as it is the principal task of the boards of appeal to review the decision under appeal on the basis of the appellant's requests. In such case, the board must carry out a substantive examination of the opposition division's decision and can only set aside this decision if the grounds for opposition which led to

revocation of the patent do not prejudice the maintenance of the patent.

- 1.2 In the circumstances of the present case, the sole ground of revocation is lack of inventive step for each of the operative requests.

Main request (patent as granted)

2. Inventive step

- 2.1 Closest prior art

- 2.1.1 According to the EPO case law, the closest prior art for assessing inventive step is a prior art disclosing subject matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common, i.e. requiring the minimum of structural modifications (Case Law, *supra*, I.D.3.1).

- 2.1.2 The appellant argued that D3 should be considered as the closest prior art document and not D1, as was done by the opposition division. In particular, the appellant held that D3 was a more suitable closest prior art than D1 because it shared more technical features in common with granted claim 1, in particular because D3 disclosed some information in respect of the degree of O-acetylation (page 19, line 17; page 20, line 17), which was not the case for D1.

- 2.1.3 However, the patent in suit (claims 1, 2, 5, 10, 25, 26; paragraphs 1-4, 11, 149-164, 169-172) and both D1 (claims 6, 14, 30-37, 42, 43, 49, 59; page 1, lines 4 and 29-32; page 4, lines 12-16; page 14, lines 2-9; page 16, line 8 to page 19, line 15; page 20, both

complete tables; page 22-29, sections G, H, J) and D3 (claims 1, 9, 25; page 1, lines 4-8; page 6, lines 7-15; page 7, line 15; examples 1 and 4-7) are in the field of vaccines and all three relate specifically to Men W135 and Men Y conjugates for inducing immune responses.

2.1.4 The Board is further persuaded that the indication "OAc" and "+" and "-" in the table on page 20 of D1 (Results for Men W135) together with the methods of preparation of the Men W135 and Men Y conjugates disclosed in D1 (page 17, lines 16-17 and page 18, lines 6-7 in combination with the passages at page 15, line 20 to page 16, line 7), which are, as already indicated by the opposition division, essentially the same as the one in the patent in suit (contested decision: page 9, first full paragraph), would be understood by the skilled person as an indication that the conjugates mentioned in said tables on page 20 of D1 are acetylated. In that respect, it is in particular indicated at page 17, lines 16-17 and at page 18, line 6 of D1 that the type W135 and the type Y polysaccharides prepared in the examples of D1 (and reported in the tables on page 20 thereof) are derivatised to active esters. It is further noted that although that issue had been addressed in the Board's communication (section 6.1.4), no information or argument was provided by the appellant in reply.

2.1.5 It is further noted that the appellant argued in respect of inventive step that D3 did not contain evidence that the conjugates prepared therein were capable of inducing a functional immune response (i.e. a bactericidal response which is therefore expected to prevent infection: section 2.22 of the statement of grounds of appeal). To the contrary, D1 contains some

information in that respect (see both complete tables on page 20 together with page 19, lines 10-15).

Therefore, in the Board's view, the technical effects shown in D1 are closer to those of the patent in suit than those of D3.

- 2.1.6 In view of the above, there is no apparent reason to conclude that D1 is not an appropriate starting point for the assessment of the inventive step and it is not justified that the opposition division's decision in that respect be overturned by the Board.
- 2.1.7 Therefore, D1 is considered hereinafter as the closest prior art document, whereby the tables on page 20 thereof, which are related to Men W135 and Men Y conjugates, are particularly relevant starting points for the assessment of the inventive step of the subject-matter of claims 1 and 2 of the main request, respectively.
- 2.2 Distinguishing feature(s) over D1
 - 2.2.1 The opposition division held that the distinguishing feature between the subject-matter of claims 1 or 2 of the main request and D1 was that D1 failed to disclose either explicitly or implicitly the specifically required levels of acetylation.
 - 2.2.2 The appellant argued that the opposition division's conclusion in that respect was based on hindsight because D1 did not disclose any acetylation levels at any position in the final conjugates. Therefore, the distinguishing features over D1 were in fact the levels of O-acetylation and their position *per se*.

2.2.3 However, in the Board's view, the skilled person would understand from D1 as a whole that, although D1 fails to disclose any information regarding the level of O-acetylation of the polysaccharides, an O-acetylation reaction is effectively carried out in the examples of D1 illustrated in the tables on page 20 related to Men W135 and Men Y conjugates (see section 2.1.4 above).

Besides, in view of the similarity of the preparation processes used in D1 and in the patent in suit, and in the absence of any evidence to the contrary put forward by the appellant in appeal, there is no reason to deviate from the opposition division's conclusion according to which the same O-acetylation process occurs in the examples of the patent in suit as in the ones carried out in D1. Therefore the appellant's argument according to which the position of the O-acetylation distinguished the subject-matter being claimed from D1 fails to convince.

2.2.4 Under those circumstances, there is no reason to deviate from the opposition division's conclusion (section 2.2.1).

2.3 Problem effectively solved over the closest prior art

2.3.1 The appellant argued that it was derivable from Figures 3 to 6 as well as from paragraphs 170 to 172 of the patent in suit that the technical problem was to provide improved Men W135 and Men Y conjugates that induced an effective immune response and were better defined.

2.3.2 However, no comparison between a conjugate according to claims 1 and 2 of the main request with one according

to the closest prior art (D1: tables on page 20) is present on file. There is also no evidence on file showing that a technical effect was present in relation to the specific ranges of O-acetylation at either the 7 or the 9 position defined in claims 1 and 2 of the main request.

2.3.3 Under those circumstances, the problem effectively solved over D1 formulated by the appellant in terms of an improvement over the closest prior art is not acceptable. Rather, it is agreed with the opposition division that the technical problem solved over the closest prior art resides in the provision of further conjugates that induce an effective immune response. In that respect, it is taken into account that it is shown in the last column of the tables on page 20 of D1 that both the Men W135 and the Men Y conjugates indicated therein exhibited a bactericidal activity.

2.4 Obviousness

2.4.1 The question remains to be answered if the skilled person, desiring to solve the problem identified in section 2.3.3 above, would, in view of the prior art, have modified the disclosure of the closest prior art in such a way as to arrive at the subject matter of operative claims 1 and 2.

2.4.2 In that respect, it is agreed with the appellant that the teaching of the prior art regarding the importance of the O-acetylation of Men W135 and Men Y conjugates was confused at the priority date of the patent in suit (see e.g. paragraphs 7-9 of the patent in suit as well as the passages of D2, D5, D14 cited in sections 2.9 to 2.11 of the statement of grounds of appeal).

The same conclusion is further reached in view of D24, which was submitted together with the statement of grounds of appeal in order to strengthen the appellant's line of argumentation on inventive step based on D1 defended during the opposition proceedings (see in particular section 3.1 of the statement of grounds of appeal) but which did not convince the opposition division. Under these circumstances, it would not be justified for the Board to hold D24 inadmissible pursuant to Article 12(4) RPBA.

- 2.4.3 However, in the absence of any evidence that the selection of the ranges of O-acetylation defined in granted claims 1 and 2 plays a role, these ranges cannot be held to contribute to an inventive step, but are seen to constitute a mere arbitrary distinction from the closest prior art.

Although it is indicated in D24 that O-acetylation may reduce immunogenicity (see passage of the abstract on page 1 reading "The immune response in mice was highly dependent on the degree of O-acetylation. Less O-acetylation resulted in higher serum bactericidal activity..." and "The dOA form of the vaccine may therefore provide better protection"), the teaching of D24 is specifically directed to Men C conjugates (see title, abstract) and it was neither shown, not even argued, that there was any reason to expect that the teaching of D24 would equally apply to Men W135 and Men Y conjugates (whereby Men C is known in the art to exhibit a different structure than Men W135 and Men Y) according to granted claims 1 and 2. Besides, since the teaching of D24 is that a higher degree of O-acetylation is related to lower immunogenicity, its teaching would not prevent the skilled person to use O-acetylated conjugates at all in order to solve the

problem identified above, which resides in the provision of alternative Men W135 and Men Y conjugates to the ones according to D1. Therefore, the appellant's argument according to which D24 taught away from the subject-matter according to granted claims 1 and 2 is not convincing. Rather, in the Board's view, D24 merely shows that the teaching of the prior art regarding the importance of the O-acetylation of Men conjugates was confused at the priority date of the patent in suit (see section 2.4.2 above).

Under those circumstances, it is agreed with the opposition division that, in order to provide mere alternative Men W135 and Men Y conjugates to the ones according to D1, it was obvious for the skilled person to use any polysaccharide, including those used in the patent in suit. Therefore, also in that respect, the arguments put forward by the appellant in appeal provide no reason for the Board to overturn the opposition division's decision, whereby that decision applies equally to each of claims 1 and 2 of the main request.

2.4.4 In its statement of grounds of appeal, the appellant made reference to D20 and D21 as prior art documents. However, in view of the priority date (2 October 2003) and of the filing date of the patent in suit (4 October 2004), the question arose if D20 (accepted on 10 September 2003 and apparently published in 2004: see headnote and footnote on page) and D21 (published in November 2003: see footnote on page 1), were valid prior art documents. Although that issue was identified in the Board's communication (section 4.3), whereby it was further indicated that the burden of proof was on the party relying on those documents, no information was provided by the appellant in reply. Therefore, in

the circumstances of the present case, D20 and D21 were not shown to be valid prior art documents and the appellant's arguments based on D20 and D21 are rejected.

Auxiliary requests

3. Auxiliary request 1

3.1 As compared to claims 1 and 2 of the main request, claims 1 and 2 of auxiliary request 1 were amended in order to indicate that the carrier protein was a CRM₁₉₇ carrier protein.

3.2 However, since the Men W135 and the Men Y conjugates according to the tables on page 20 of D1 were already prepared using a CRM₁₉₇ carrier protein (D1: page 17, lines 18-22; page 18, lines 6-8), the amendments made do not introduce any further difference with respect to the tables on page 20 of D1 and therefore do not contribute to an inventive step. Further considering that the appellant did not put forward any additional argument in respect of the inventive step of auxiliary request 1 as compared to the main request, the same conclusion as for the main request has to be reached for auxiliary request 1.

4. Auxiliary request 2

Claim 1 of auxiliary request 2 is identical to claim 2 of the main request. Therefore, auxiliary request 2 is not inventive over D1 for the same reasons as outlined for the main request.

5. Auxiliary request 3

5.1 As compared to claims 1 and 2 of the main request, claims 1 and 2 of auxiliary request 3 were amended in order to indicate that the conjugates were obtainable by the introduction of an amino group into the saccharide followed by derivatisation with an adipic ester and reaction with the carrier protein.

5.2 However, since the Men W135 and the Men Y conjugates according to the tables on page 20 of D1 were already prepared using such process steps (D1: page 17, lines 16-17 and page 18, lines 6-7 in combination with the passages at page 15, line 20 to page 16, line 7), the amendments made constitute no further distinguishing feature over the closest prior art. Further considering that the appellant did not put forward any additional argument in respect of the inventive step of auxiliary request 3 as compared to the main request, the same conclusion has to be reached.

6. Auxiliary request 4

6.1 As compared to claims 1 and 2 of the main request, claims 1 and 2 of auxiliary request 4 were amended in order to delete feature (b) thereof.

6.2 However, it was neither shown nor argued that the amendments made introduced any further difference with respect to the tables on page 20 of D1. Therefore, in particular in the absence of any additional argument in respect of the inventive step of auxiliary request 4 as compared to the main request, the same conclusion as for the main request has to be reached for auxiliary request 4.

7. Since neither the main request, nor any of auxiliary requests 1 to 4 is inventive, the appeal is to be dismissed.

Order

For these reasons it is decided that:

The appeal is dismissed

The Registrar:

The Chairman:



L. Malécot-Grob

D. Semino

Decision electronically authenticated