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Datasheet for the decision of 17 December 2012

Case Number: T 1728/08 - 3.3.04

Application Number: 96303835.1

Publication Number: 745387

IPC: A61K 39/39

Language of the proceedings: EN

Title of invention:
Adjuvants for viral vaccines

Patentee:
Wyeth LLC

Opponent:
SOCIETE D'EXPLOITATION DE PRODUITS POUR L'INDUSTRIE CHIMIQUE, S.E.P.P.I.C.

Headword:
Adjuvants/WYETH

Relevant legal provisions:
EPC Art. 54, 56, 84
RPBA Art. 12(4), 13(1)

Keyword:
"Main request - novelty (no)"
"Auxiliary request 1 - clarity (no)"
"Auxiliary request 2 - inventive step (no)"
"Auxiliary request 3 - not admitted"

Decisions cited:
-

Catchword:
-

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Case Number: T 1728/08 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 17 December 2012

Appellant: (Opponent)
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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 9 July 2008 concerning maintenance of European patent No. 745387 in amended form.

Composition of the Board:

Chairman: C. Rennie-Smith
Members: B. Claes
M. Montrone

Summary of Facts and Submissions

I. The appeal was lodged by the opponent (appellant) against the interlocutory decision of the opposition division according to which European patent No. 0 745 387 (entitled "*Adjuvants for viral vaccines*" which was granted with 18 claims on European patent application 96303835.1) could be maintained in amended form on the basis of claims 1 to 13 as granted.

II. Claim 1 as granted read:

"1. A mammalian vaccine composition comprising an inactivated whole or subunit vaccine and an effective amount of an adjuvant, characterised in that the adjuvant comprises squalene or squalane or a mixture thereof, glycerol and a surfactant."

III. The opposition was filed on the grounds as set forth in Articles 100(a) (lack of novelty, Article 54 EPC and lack of inventive step, Article 56 EPC) and 100(b) EPC.

IV. The documents cited in the present decision are:

D0: GB 2 189 141

D1: GB 2 189 143

D7: US 5,376,369

D10: WO 94/20071

V. A notice of appeal and a statement setting out the grounds of appeal dated 7 November 2008 were filed by

the appellant. The statement contained facts and arguments to the effect that claim 1 as granted lacked novelty (Article 54 EPC) over the disclosure in a newly cited document (D0) and lacked inventive step, partially based on a newly filed document (D10).

VI. On 1 April 2009, the respondent (patent proprietor) filed a reply to the grounds of appeal and requested that the appeal be dismissed.

VII. Oral proceedings before the board were held on 17 December 2012. During these oral proceedings the respondent filed three auxiliary requests.

Claim 1 of auxiliary request 1 was to the mammalian vaccine as in claim 1 as granted wherein the surfactant was defined as "selected from Polysorbate 20, Polysorbate 60, Span 80 Sorbitan Oleate, Cremophor® surfactants and polysorbate 80".

Claim 1 of auxiliary request 2 was to the mammalian vaccine as in claim 1 as granted wherein the surfactant was defined as "which is polysorbate 80".

Claim 1 of auxiliary request 3 read:

"1. A mammalian vaccine composition comprising an inactivated whole or subunit vaccine and an effective amount of an adjuvant, characterised in that the adjuvant contains 5% squalene 20% glycerol and 0,2% Tween80 (% by volume of the final composition)."

VIII. The appellant's arguments as far as they are relevant for the present decision can be summarised as follows:

Main request - claim 1 - novelty (Article 54 EPC)

– Document (D0) disclosed on page 2 in lines 22 to 24 and 28 a mammalian vaccine composition comprising compounds as disclosed in claim 1.

Auxiliary request 1

Admissibility

– Auxiliary request 1 should not be admitted into the proceedings as it was only filed at the oral proceedings and not with the respondent's reply.

Claim 1 - clarity (Article 84 EPC)

– The words "Cremophor® surfactants" in this request did not relate to a structurally unambiguously defined surfactant species and were therefore not clear within the meaning of Article 84 EPC.

Auxiliary request 2

Admissibility

– Auxiliary request 2 should not be admitted into the proceedings as it was only filed at the oral proceedings and not with the respondent's reply.

Claim 1 - inventive step (Article 56 EPC)

– The closest prior art was represented by either document (D0), (D1) or (D7).

– Starting from (D0) as closest prior art, the only technical difference with the claimed invention was the use of polysorbate 80 instead of lecithin as surfactant. The use of Tween 80 (polysorbate 80) was however known from document (D7) as disclosed for instance in column 9, line 20. The subject-matter of claim 1 therefore lacked inventive step.

Auxiliary request 3 - admissibility

– This request was late filed at the end of the oral proceedings. The request required a full examination of its compliance with the EPC, not least because the additional features were taken from the description. There were no "exceptional" circumstances justifying the late filing of this request. The board should find the request inadmissible.

IX. The respondent's arguments as far as they are relevant for the present decision can be summarised as follows:

Main request - claim 1 - novelty (Article 54 EPC)

– Document (D0) disclosed an immunological adjuvant containing a lipid emulsion system, comprising a metabolisable oil, a low molecular weight polyol and lecithin, and at least one refined detoxified bacterial biological adjuvant. In order to obtain the subject-matter of claim 1 from the disclosure in document (D0) it was necessary to select squalene from a list of seven possible named oils (including making a selection between vegetable

and animal oils) and to select a polyol from glycerol and seven other mentioned polyols. None of the claims as originally filed singled out glycerin as being more suitable than the others.

– The skilled man moreover needed to omit RDE, i.e. the explicitly mentioned refined detoxified bacterial biological adjuvant, from the formulation in document (D0) as this was an adjuvant in its own right and considered to be an essential component of the prior art formulation. It was indeed clear from table 1 on page 4 of document (D0) that RDE was the major compound in the disclosed compositions having adjuvant activity.

Auxiliary request 1

Admissibility

– The amendment to claim 1 was based on page 3, lines 1 to 5 of the application as published. The claim was largely identical to claim 1 of the auxiliary request pending before the opposition division. The amendment could therefore not come as a surprise to the appellant. Accordingly, auxiliary request 1 should be allowed into the proceedings.

Claim 1 - clarity (Article 84 EPC)

– The trademark Cremophor® had been used for decades in the relevant technical field and was perfectly clear to a skilled person. The words Cremophor®

surfactants were devoid of any ambiguity. The amendment was therefore clear and complied with Article 84 EPC.

Auxiliary request 2

Admissibility

– The amendment to claim 1 was based on page 3, lines 3 of the application as published. The claim was identical to claim 2 of the auxiliary request pending before the opposition division. The amendment could therefore not come as a surprise to the appellant. Accordingly, auxiliary request 2 should be allowed into the proceedings.

Claim 1 - inventive step (Article 56 EPC)

– All the adjuvants disclosed in document (D0) and (D1) contained RDE, i.e. they explicitly mentioned refined detoxified bacterial biological adjuvant for the formulation of the vaccines. There was no teaching in these documents that the emulsion adjuvants could be used while omitting RDE.

– All the adjuvants disclosed in document (D7) taught the use of N-acetyl-muramyl-L-threonyl-D-isoglutamine. The skilled person would therefore refrain from formulating any adjuvants based on the teaching of document (D7) which would omit that compound.

Auxiliary request 3 - admissibility

– The third auxiliary request was based on example two of the description of the application as published. It was a *bona fide* attempt to overcome the objections of the board to the higher ranking claim requests.

X. The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

The respondent (patent proprietor) requested that the appeal be dismissed or that the decision under appeal be set aside and the patent be maintained on the basis of one of three auxiliary requests filed during the oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

Admissibility of document (D0) and (D10) into the proceedings

2. The respondent explicitly consented to the introduction into the proceedings of documents (D0) and (D10), both first cited by the appellant with the statement setting out the grounds of appeal. The board therefore considers that there is no need to exercise its discretion provided under Article 12(4) RPBA. These documents are therefore considered in the present decision.

Main request - claim 1 - novelty (Article 54 EPC)

3. On page 1 in lines 5 to 7, document (D0) discloses that the "*invention is directed to an immunological adjuvant system which enhances the immune response against antigens, and hence is useful in vaccines*." On lines 44 to 51 document (D0) specifies that the immunological adjuvant "*is comprised of:*
1. A lipid emulsion system (LES) containing:
(a) a metabolizable oil,
(b) a low molecular weight polyol,
(c) lecithin, and
2. A refined detoxified bacterial biological adjuvant, which may be, but is not limited to refined detoxified endotoxin (RDE), trehalose dimycolate (TDM), protein from Salmonella typhimurium (STM), and the like".

It is stated in particular on page 2, lines 23 to 28 that the lipid emulsion system (LES) contains "*a metabolizable oil, a low molecular weight polyol, such as* ***glycerin****, and lecithin. In practice, it has been found that the metabolizable oil is preferably a fatty oil comprises mainly of diglycerides and triglycerides of oleic and inoleic acids. Particularly preferred are the fatty vegetable oils such as those contained in, or obtained from, peanut oil, sunflower seed oil safflower seed oil, corn oil and the like. Other oils such as olive oil, cottonseed oil or* ***squalene*** *can also be employed in the adjuvants of the present invention.*" (emphasis added by the board). That the LES as described in document (D0) are applied in mammalian (mice) vaccines comprising a whole or subunit vaccine (foot and mouth disease virus synthetic peptide) can be taken from at least example 1 in the document.

Accordingly, the board is satisfied that document (D0) discloses a mammalian vaccine as defined in claim 1 as granted.

4. The respondent has argued that in order to obtain from the disclosure in document (D0) an immunological adjuvant as defined in the claims, the skilled person would have to make two choices from two separate lists, i.e. squalene needed to be selected from a list of seven possible named oils and glycerol needed to be selected from a list of eight mentioned polyols. Furthermore, none of the claims as originally filed singled out glycerin as being more suitable than the others.

5. The board however cannot accept this argument. From the passages of document (D0) mentioned in point 3, above, the paragraph on page 2 in lines 23 to 24 ("*a metabolizable oil, a low molecular weight polyol, such as* ***glycerin****, and lecithin.*"), unambiguously singles out glycerol (glycerine) and lecithin (surfactant) as the latter two compounds of the disclosed adjuvant. Accordingly, unlike the argument of the respondent, in order to obtain from the cited passages the adjuvant as defined in claim 1, the skilled person only has to make a single choice from the relatively short list of metabolizable oils including squalene as mentioned in the following passages. This argument must therefore fail.

6. The respondent has furthermore argued that the skilled person needed to omit RDE, i.e. the explicitly mentioned refined detoxified bacterial biological

adjuvant, from the formulation in document (D0) in order to obtain the vaccine as claimed. RDE was however an adjuvant in its own right and a major compound with adjuvant activity in the disclosed formulation.

7. The board notes that claim 1 is directed to a mammalian vaccine *comprising* certain compounds. Accordingly, the wording of the claim does not exclude the presence in the claimed vaccine of other compounds than those explicitly mentioned. Therefore the board considers it to be of no relevance in this context whether or not the skilled person would include RDE in the vaccine. This argument must therefore fail also.

8. In view of the above considerations the board concludes that the subject-matter of claim 1 is not novel (Article 54 EPC) over the disclosure in document (D0).

Auxiliary request 1

Admissibility

9. Auxiliary request 1 was only filed at the oral proceedings after it became clear to the respondent that the board was considered the main and sole request before it to contravene Article 54 EPC.

10. Claim 1, which is similar to claim 1 of the auxiliary request which was pending before the opposition division, now mentions a number of surfactants from which the surfactant of the adjuvant as defined in claim 1 may be selected. Lecithin, the surfactant disclosed in document (D0), is no longer present. Accordingly, in view of the possibly novelty

establishing character of the amendment and the late filing of the potentially novelty destroying document (D0), the board exercises its discretion under Article 13(1) RPBA in favour of the respondent.

11. Auxiliary request 1 is therefore admitted into the proceedings.

Claim 1 - clarity (Article 84 EPC)

12. The amendment to claim 1 introduces the notion "Cremophor® surfactants" as a possibly selected surfactant in the adjuvant as defined. However, these trademarked surfactants do not relate to a structurally unambiguously defined surfactant species, but rather to a host of differently structured alternatives produced by the BASF Corporation, Parsippany, NJ (see page 3, line 3 of the application as published). The host of alternatives covered by the trademark is not considered to be defined and fixed and therefore the board cannot be satisfied that the subject-matter of a claim relying on this trademark can comply with the requirement of clarity within the meaning of Article 84 EPC.

Auxiliary request 2

Admissibility

13. Auxiliary request 2 was also only filed at the oral proceedings after it became clear to the respondent that the main and auxiliary request 1 were considered by the board to contravene Article 54 EPC and Article 84 EPC, respectively.

14. Claim 1 of auxiliary request 2 is restricted to one particular embodiment falling within claim 1 of auxiliary request 1 and mentions a number of surfactants from which the surfactant of the adjuvant as defined in claim 1 may be selected. "Cremophor® surfactants" are no longer mentioned. Moreover, claim 1 of auxiliary request 2 is identical to claim 2 of the auxiliary request which was pending before the opposition division. Accordingly, in view of the obvious clarity establishing character of the amendment the board exercises its discretion under Article 13(1) RPBA in favour of the respondent.

15. Auxiliary request 2 is therefore admitted into the proceedings.

Claim 1 - inventive step (Article 56 EPC)

Closest prior art

16. In assessing whether or not a claimed invention meets the requirements of Article 56 EPC, the boards of appeal apply the "problem and solution" approach, which requires as a first step the identification of the closest prior art. In accordance with the established case law of the boards of appeal, the closest prior art is a teaching in a document 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 to arrive at the claimed invention.

17. On the basis of these requirements the board considers document (D0) to represent the closest prior art rather than document (D1) as argued by the respondent. Although both documents disclose (see document (D0), page 2, lines 22 to 37; see document (D1), page 2, lines 5 to 20) vaccines comprising an adjuvant based on a LES component which is composed of a metabolizable oil, a low molecular weight polyol and a surfactant, the LES component as disclosed in document (D0) is structurally more similar to the adjuvant as defined in claim 1 than that in document (D1) as there is a concrete disclosure of a LES adjuvant comprising squalene, glycerol and the surfactant lecithin (see point 3, above). The board considers this disclosure in document (D0) moreover as a closer prior art than the oil-in-water emulsion system as disclosed in document (D1) on page 2, line 42 to 52, as the latter is merely restricted to a two compound system, comprising e.g. squalene and a detergent such as Tween-80 (i.e. polysorbate 80) as opposed to the three compound system as disclosed in document (D0) and the system as defined in claim 1.

Problem to be solved

18. The difference between the vaccine comprising the LES system as disclosed in document (D0) and the vaccine as subject-matter of claim 1 is the use of the surfactant polysorbate 80 (a.k.a. Tween-80) instead of lecithin. The patent does not comprise any indication that the vaccine of or the adjuvant defined in claim 1 have any advantageous or surprising effects over any of the prior art compounds which is attributable to the

specific use of polysorbol 80 nor has the respondent argued along those lines.

19. Accordingly, the objective technical problem to be solved by the subject-matter of claim 1 is the provision of an alternative lipid emulsion system (LES) system to that disclosed in document (D0) for use in mammalian vaccines.

20. The board is satisfied that the examples of the patent demonstrate that the claimed subject-matter solves this problem.

Obviousness

21. Document (D7) concerns vaccines comprising an adjuvant composition in the form of an emulsion comprising a non-toxic tetra-polyol, a non-toxic metabolizable oil and a glycol ether based surfactant (see e.g. column 9 lines 31 to 38). Document (D7) discloses a preferred adjuvant comprising a particular tetra-polyol, squalene (or squalane) and Tween® 80 (see column 9 line 64 to column 10 line 9; column 10 line 40 to 49, column 11 lines 34 to 44 and column 12, lines 34 to 40). Document (D7) therefore discloses the use of Tween® 80 (polysorbate 80) in vaccine emulsion adjuvants which further comprise a polyol and squalene. The board is therefore satisfied that, when embarking on solving the objective technical problem defined above, the skilled person would consider the substitution of lecithin for polysorbate 80 in the adjuvants disclosed in document (D0) obvious in the light of the teaching in document (D7).

22. The respondent has argued, much as it did in the context of novelty, that the adjuvants disclosed in document (D0) explicitly mentioned the additional use of refined detoxified bacterial biological adjuvant and that there was no teaching in the document that emulsion adjuvants could be used which did not contain RDE. A similar argument was submitted in the context of the disclosure in document (D7), i.e. that all adjuvants disclosed therein taught the use of N-acetyl-muramyl-L-threonyl-D-isoglutamine.

23. The board refers however to point 7, above, in which it was considered that the wording of the claim does not exclude the presence in the claimed vaccine of other compounds than those explicitly mentioned. Therefore the board considers that in this context also, it is of no relevance whether or not the skilled person would include RDE or N-acetyl-muramyl-L-threonyl-D-isoglutamine in the vaccine. This argument must therefore fail.

24. Accordingly, the subject-matter of claim 1 is rendered obvious by the prior art and therefore lacks inventive step (Article 56 EPC).

Auxiliary request 3 - admissibility

25. The respondent requested the board to admit auxiliary request 3 at the end of the oral proceedings after the board had successively admitted auxiliary requests 1 and 2 and in each case found them not allowable.

26. The respondent indicated that claim 1 of auxiliary request 3 was supported by example 2 in the description

of the application as published. Whereas claim 1 of each of auxiliary requests 1 and 2 had been similar to claims which had been contained in the auxiliary request which was pending before the opposition division (see points 10 and 14, above) the subject-matter of claim 1 of auxiliary request 3 had never been considered in these opposition or appeal proceedings.

27. The result of admitting auxiliary request 3 into the proceedings would be a situation in which the parties to these opposition proceedings and the board, just before finalising the present appeal and at an extremely late stage of the proceedings, would have to consider anew the requirements of the EPC or possibly even remit the case to the first instance for further prosecution on the basis of this request.

28. Circumstances which could justify the exceptional treatment of this auxiliary request could not be brought forward by the respondent. The board can also not identify any such circumstances.

29. The board cannot therefore see how its discretion can be exercised in favour of the respondent to allow auxiliary request 3 into the proceedings in view of "the current state of the proceedings" (see Article 13(1) RPBA).

30. In view of the above considerations, the board decides that auxiliary request 3 filed by the respondent during the oral proceedings is not admissible.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar The Chairman

P. Cremona C. Rennie-Smith