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Datasheet for the decision of 29 March 2012

Case Number: T 1034/08 - 3.3.02

Application Number: 00907228.1

Publication Number: 1156781

IPC: A61K 9/107, A61K 9/00

Language of the proceedings: EN

Title of invention:
Microemulsions with adsorbed macromolecules and microparticles

Patentee:
Novartis Vaccines and Diagnostics, Inc.

Opponent:
GlaxoSmithKline Biologicals SA

Headword:
Microemulsions with adsorbed macromolecules and microparticles/NOVARTIS VACCINES AND DIAGNOSTICS, INC.

Relevant legal provisions:
EPC Art. 123(2)(3)
EPC R. 77, 101
RPBA Art. 13

Keyword:
"Admissibility of opposition - (yes): opponent clearly identifiable"
"All requests - allowability of amendments - (no): new specific combinations"
"Auxiliary requests I to V - extension of the protection conferred - (yes)"

Decisions cited:
-

Catchword:
-

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Case Number: T 1034/08 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 29 March 2012

Appellant-Proprietor: (Patent Proprietor)
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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 27 March 2008 concerning maintenance of European patent No. 1156781 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: A. Lindner
D. Prietzel-Funk

Summary of Facts and Submissions

I. European patent No. 1 156 781 based on application No. 00 907 228.1 was granted on the basis of 49 claims. Independent claim 1 reads as follows:

"1. An emulsion comprising droplets less than 1 µm diameter and having an adsorbent surface, said emulsion comprising:

(a) a metabolizable oil;

(b) an emulsifying agent, comprising an ionic detergent; and

(c) at least one a biologically active macromolecule selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant,

wherein said biologically active macromolecule is adsorbed on the surface of the emulsion."

II. An opposition was filed against the patent by "GSK Biologicals SA". The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step, under Article 100(b) EPC for insufficiency of disclosure and under Article 100(c) EPC for amendments that contained subject-matter extending beyond the content of the application as originally filed.

III. The present appeals lie from a decision of the opposition division pronounced on 26 February 2008 and

posted on 27 March 2008, wherein the European patent was maintained on the basis of auxiliary request VIII. In said decision, the opposition division decided that the opposition was admissible, in particular as the identity of the opponent could clearly be established. Moreover, the opposition division came to the conclusion that the main request as well as auxiliary requests II to IV and VI did not meet the requirements of Article 123(2) EPC and that the subject-matter of auxiliary requests I, V and VII lacked novelty.

Regarding auxiliary request VIII, the subject-matter claimed therein was found to meet the requirements of Article 123(2) EPC. Furthermore, novelty as well as inventive step were acknowledged.

IV. Both parties lodged an appeal against that decision.

V. In the statement of the grounds of appeal dated 6 August 2008, the appellant-proprietor contested *inter alia* the admissibility of the opposition and also of appellant-opponent's appeal. As an auxiliary measure it submitted auxiliary requests I to V.

VI. In the annex to the summons to oral proceedings issued pursuant to Article 15(1) RPBA, the board gave its preliminary opinion regarding the admissibility of appellant-opponent's appeal and raised objections under Article 123(2) EPC in connection with auxiliary requests I to V.

VII. With letter dated 29 February 2012, the appellant-proprietor filed auxiliary requests I to IX. The

relevant independent product claims of auxiliary requests I to V read as follows:

(i) Auxiliary request I

"1. An emulsion comprising oil droplets and having an adsorbent surface, wherein at least 80% (by number) of the droplets are less than 1 micron in diameter, said emulsion comprising:

(a) a metabolizable oil;

(b) an emulsifying agent, comprising an anionic detergent; and

(c) at least one biologically active macromolecule which is a polypeptide, wherein said biologically active macromolecule is adsorbed on the surface of the emulsion.

2. An emulsion comprising oil droplets and having an adsorbent surface, wherein at least 80% (by number) of the droplets are less than 1 micron in diameter, said emulsion comprising:

(a) a metabolizable oil;

(b) an emulsifying agent, comprising a cationic detergent; and

(c) at least one biologically active macromolecule which is a polynucleotide, wherein said biologically active macromolecule is adsorbed on the surface of the emulsion, for use in stimulating an immune response in a host animal.

3. An emulsion comprising oil droplets and having an adsorbent surface, wherein at least 80% (by number) of the droplets are less than 1 micron in diameter, said emulsion comprising:

(a) a metabolizable oil;
(b) an emulsifying agent, comprising a cationic detergent; and
(c) at least one biologically active macromolecule which is a CpG oligonucleotide, wherein said biologically active macromolecule is adsorbed on the surface of the emulsion.

4. An emulsion comprising oil droplets and having an adsorbent surface, wherein at least 80% (by number) of the droplets are less than 1 micron in diameter, said emulsion comprising:
(a) squalene;
(b) an emulsifying agent, comprising a cationic detergent; and
(c) at least one biologically active macromolecule which is a polynucleotide, wherein said biologically active macromolecule is adsorbed on the surface of the emulsion.

(ii) Auxiliary request II

"1. An emulsion comprising oil droplets and having an adsorbent surface, wherein at least 80% (by number) of the droplets are less than 1 micron in diameter, said emulsion comprising:
(a) a metabolizable oil;
(b) an emulsifying agent, comprising an anionic detergent; and
(c) at least one biologically active macromolecule which is a protein, wherein said biologically active macromolecule is adsorbed on the surface of the emulsion."

Independent claims 2 to 4 are identical to claims 2 to 4 ofauxiliary request I.

(iii) Auxiliary request III

Independent claims 1 to 3 are identical to claims 2 to 4 of auxiliary request I.

(iv) Auxiliary request IV

Independent claims 1 to 3 are identical to claims 1 to 3 of auxiliary request I.

(v) Auxiliary request V

Independent claims 1 to 2 are identical to claims 2 to 3 of auxiliary request I.

VIII. At the oral proceedings, which were held on 29 March 2012, the appellant-proprietor withdrew auxiliary requests VI to IX, filed with letter dated 29 February 2012, and submitted new auxiliary requests VI and VII. The relevant claims read as follows:

(i) Auxiliary request VI

Independent claim 1 is identical to claim 1 of auxiliary request II.

"2. An emulsion comprising oil droplets and having an adsorbent surface, wherein at least 80% (by number) of the droplets are less than 1 micron in diameter, said emulsion comprising:
(a) a metabolizable oil;

(b) an emulsifying agent, comprising a cationic detergent; and

(c) at least one biologically active macromolecule which is an adjuvant and which is a CpG oligonucleotide, wherein said biologically active macromolecule is adsorbed on the surface of the emulsion.

8. The emulsion of any preceding claim, wherein said emulsifying agent further comprises a non-ionic detergent."

(ii) Auxiliary request VII

Independent claim 1 is identical to claim 2 of auxiliary request VI.

"7. The emulsion of any preceding claim, wherein said emulsifying agent further comprises a non-ionic detergent."

IX. In connection with the admissibility of the appellant-opponent's opposition and the appeal as well as the allowability of the amendments under Article 123(2) and (3) EPC, the appellant-proprietor essentially argued as follows:

Regarding the admissibility of the opposition and the appellant-opponent's subsequent appeal, the appellant-proprietor argued that the opposition had been filed by "GSK Biologicals S.A.". However, there was no such legal entity. Furthermore, the appeal had been filed in the name of "GlaxoSmithKline Biologicals s.a.". This meant that either the original opposition was

inadmissible because the legal entity "GSK Biologicals S.A." did not exist, or, alternatively, the appeal was inadmissible because it had not been filed in the name of the person adversely affected by the opposition division's decision.

Regarding the basis for the term polypeptide on page 29 of the original application, reference was made to the second paragraph of page 14 of the original application, according to which "[t]he terms "polypeptide" and "protein" refer to a polymer of amino acid residues and are not limited to a minimum length of the product". As a consequence, the terms polypeptide and protein were identical and could therefore be used interchangeably.

The appellant-proprietor repeatedly made reference to pages 9 and 29 as the basis for the amendments introduced into the present claims.

X. With regard to the admissibility of its opposition and its appeal as well as the allowability of the amendments under Article 123(2) and (3) EPC, the appellant-opponent essentially argued as follows:

Regarding the admissibility of the opposition and the appellant-opponent's subsequent appeal, the appellant-opponent argued that, in view of the fact that "GSK" was a well-known abbreviation of "GlaxoSmithKline" and that the address provided in the Notice of Opposition matched that of "GlaxoSmithKline Biologicals", there could be no doubt that "GSK Biologicals" and "GlaxoSmithKline Biologicals" were the same legal entity.

In connection with the requirements of Article 123(2) EPC, it was essentially argued that although the newly features as such were all originally disclosed, their combination did not have a basis in the original application. These unallowable combinations were not only present in the independent claims of all requests, but also in the respective combinations of independent and dependent claims. Reference in this context was made to claims 1 plus 8 and 2 plus 8 of auxiliary request VI and claims 1 plus 7 of auxiliary request VII.

In view of the fact that the CpG oligonucleotides of claim 3 of auxiliary request I were not limited to macromolecules suitable as adjuvants, there was an extension of the scope of protection. The requirements of Article 123(3) EPC were therefore not met.

XI. The appellant-proprietor requested that the decision under appeal be set aside and the opposition be rejected as inadmissible. Alternatively, it requested that the decision under appeal be set aside and the patent be maintained on the basis of auxiliary requests I to V, all filed with the letter dated 29 February 2012, alternatively on the basis of auxiliary requests VI or VII submitted during the oral proceedings of 29 March 2012.

The appellant-opponent requested that the decision under appeal be set aside and that the European patent No. 1156781 be revoked. Furthermore, it requested that the auxiliary requests, filed by the appellant-proprietor with letter dated 29 February 2012 and the

auxiliary requests submitted during the oral proceedings not be admitted.

Reasons for the Decision

1. Admissibility of the opposition and the appeal filed by the appellant-opponent

A natural or legal person filing an opposition must be identifiable at the latest at the end of the opposition period. The notice of opposition was filed on behalf of GSK Biologicals SA, a legal entity having its place of business in Belgium. The notice of appeal was filed on behalf of GlaxoSmithKline Biologicals SA. Both GSK Biologicals SA and GlaxoSmithKline Biologicals SA have the same address. In principle, the use of an abbreviation instead of the full name of a legal entity does not render an opposition inadmissible, as long as the party's identity can be established. In the view of the board there remains no reasonable doubt that the abbreviation GSK stands for GlaxoSmithKline. In this context, reference is made to the Certificate of the associated notaries Vroninks & Rickers of 27 February 2012, submitted by the appellant-opponent with letter dated 29 February 2012, according to which the Belgian Company Law allows the co-existence of more than one company name, one being the primary name and the others being(s) the alternative name(s). Said Certificate further indicates that GlaxoSmithKline Biologicals, which is the sole primary name, may be abbreviated to GSK Biologicals. The board concludes therefrom that GSK Biologicals does not constitute an incorrect designation of the opponent. The board further

concludes that the opposition and the appeal were filed by the same legal entity. As a consequence, both the opposition and the appeal filed by the appellant-proprietors are admissible (Rules 77 and 101 EPC).

2. Admission of auxiliary requests VI and VII

These requests were filed at a late stage of the oral proceedings before the board. Their admissibility is therefore at the board's discretion and depends upon the overall circumstances of the case under consideration (see Article 13 RPBA). The amendments essentially were a reaction of the appellant-proprietor to objections raised by the appellant-opponent under Article 123(3) EPC. As these objections were also raised for the first time at a rather late stage of the appeal proceedings, namely in the letter dated 29 February 2012 and as the amendments were of a simple nature which did not take the appellant-opponent by surprise or complicate the further proceedings, the board decided to admit auxiliary requests VI and VII into the proceedings (Article 13 RPBA).

3. Auxiliary request I

3.1 Claim 1 - Article 123(2) EPC

3.1.1 Claim 1 of auxiliary request I relates to oil droplet emulsions comprising a metabolizable oil, an emulsifying agent comprising an anionic detergent and a biologically active macromolecule in the form of a polypeptide. The appellant-proprietor cited page 29 of the original application as basis for the subject-matter of that claim, which in the third sentence of

the first paragraph discloses oil droplet emulsions comprising a metabolizable oil and an emulsifying agent. According to the fifth sentence of said paragraph, the emulsion is preferably positively charged as a result of a cationic detergent being used as the emulsifying agent or, alternatively, contains a cationic detergent being used as the emulsifying agent. Finally, the last sentence of the first paragraph discloses the alternative use of an anionic detergent if proteins are chosen as biologically active macromolecules.

However, page 29 does not relate to polypeptides. As a consequence, the specific combination of an oil droplet emulsion comprising a metabolizable oil plus an anionic detergent plus a polypeptide is not specifically disclosed in the original application, neither by explicit nor by implicit disclosure. As a consequence, the requirements of Article 123(2) EPC are not met.

3.1.2 Further arguments from the appellant-proprietor

In connection with appellant-patentee's argument that the terms polypeptide and protein can be used interchangeably, the board notes that the second paragraph on page 14 of the original application, which was cited by the appellant-patentee in this context and according to which "[t]he terms "polypeptide" and "protein" refer to a polymer of amino acid residues and are not limited to a minimum length of the product…", does indeed propose identical meanings for these terms. However, there are other passages in the original application, which indicate that they are not to be used interchangeably. Thus, the second paragraph on page 7 says that "[i]n another embodiment, the

invention is directed to such microparticles which further comprise a selected macromolecule adsorbed on the microparticle's surface, such as a pharmaceutical, a polynucleotide, **a polypeptide, a protein,** a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, an antigen, an adjuvant, or combinations thereof, and the like." [emphasis by the board]. The board concludes that a combination of a polypeptide and a protein, which is included in said embodiment, excludes the possibility of these two components being identical. In view of the fact that the basis for any amendment, no matter whether it is based on explicit or implicit disclosure, must be clear and unambiguous, and that the original application contains contradictory statements as to whether or not proteins and polypeptides are identical, this argument cannot succeed.

In this context, the appellant-proprietor also made reference to dependent claim 12 of the original application. However, the fact that anionic surfactants are individualised therein, as incidentally are cationic detergents in dependent claim 9, has no influence on the fact that the specific combination of an oil droplet emulsion comprising a metabolizable oil plus an anionic detergent plus a polypeptide is not specifically disclosed in the original application, neither by explicit nor by implicit disclosure. As a consequence, this argument cannot succeed either.

3.2 Claim 3 - Article 123(3) EPC

3.2.1 Claim 1 as granted comprises an emulsion, comprising as mandatory constituents a metabilizable oil (a), an ionic detergent (b) and a biologically active macromolecule selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant (c). Claim 3 of auxiliary request I merely requires the biologically active macromolecule to be a CpG oligonucleotide which was selected as a specific embodiment of an adjuvant. In view of the fact that not all CpG oligonucleotides are immunostimulatory and thus can act as adjuvants, the protection conferred by the patent is now extended to emulsions not containing any of the biologically active macromolecules defined in claim 1(c) as granted. As a consequence, the requirements of Article 123(3) EPC are not met.

3.2.2 Further arguments by the appellant-proprietor

Making reference to pages 5, 10 and 40 of the original application, the appellant-proprietor argued that biologically active CpG oligonucleotides essentially have immunostimulatory properties and are therefore in general suitable as adjuvants. The passages cited in this context do, however, not show that this would be the case for all CpG oligonucleotides. Thus, the sentence on page 5 at the beginning of the first full paragraph, which was particularly cited in this context (Oligonucleotides comprising CpG motifs mixed with antigens which have been demonstrated to induce strong

Th1 immune responses), has to be read in the sense of "there are oligonucleotides comprising CpG motifs mixed with antigens have been demonstrated to induce strong Th1 immune responses". Likewise, the first sentence on page 10, which was also highlighted by the appellant-proprietor, mentions preferred embodiments as does the first complete paragraph on page 40. As a consequence, the original application does not teach that all CpG oligonucleotides are suitable as adjuvants.

3.3 In view of these findings, an evaluation of the allowability of the amendments made in claims 2 and 4 is not necessary.

4. Auxiliary requests II, III and V

Claim 3 of auxiliary request II and claims 2 of auxiliary requests III and V are identical to claim 3 of auxiliary request I. As a consequence, the reasoning of point 3.2 above also applies to claim 3 of auxiliary request II and to claims 2 of auxiliary requests III and V. The requirements of Article 123(3) EPC are therefore not met.

5. Auxiliary request IV

Claims 1 and 3 of auxiliary request IV are identical to claims 1 and 3 of auxiliary request I. As a consequence, the reasoning of points 3.1 and 3.2 above also applies to claims 1 and 3 of auxiliary request IV. The requirements of Article 123(2) EPC (claim 1) and of Article 123(3) EPC (claim 3) are therefore not met.

6. Auxiliary request VI

6.1 Article 123(3) EPC

As compared to claim 3 of auxiliary request I, the CpG oligonucleotides are now limited to compounds having adjuvant functionality. The requirements of Article 123(3) EPC are therefore met.

6.2 Article 123(2) EPC

6.2.1 Claim 1 in combination with claim 8

Claim 1 in combination with claim 8 discloses a microemulsion comprising a metabolizable oil, an emulsifying agent comprising an anionic detergent and a non-ionic detergent, and a biologically active protein.

The first two sentences of the fifth paragraph of page 9 of the original application disclose microemulsions which comprise an oil droplet emulsion formulated with an ionic detergent. Such compositions readily adsorb macromolecules such as DNA, protein, and other antigenic molecules. These two sentences are then followed by a passage relating to adjuvant compositions which in turn is followed by a reference to oil droplet emulsions comprising a metabolizable oil and an emulsifying agent which are preferably present in the form of an oil-in-water emulsion having oil droplets substantially all of which are less than 1 µm in diameter. Then, further down in the same paragraph, comes the statement that the emulsifying agent preferably comprises a non-ionic detergent such as a polyoxyethylene sorbitan mono-, di-, or triester or a

sorbitan mono-, di-, or triether. It is not clear for the skilled person whether this passage constitutes a coherent description of a single product or whether it relates to the following three alternative compositions: (a) microemulsions as defined in sentences 1 and 2 of the fifth paragraph on page 9; (b) adjuvant compositions as defined in sentences 3 and 4 of said paragraph; and (c) an oil droplet emulsion as defined in sentence 5 and comprising an emulsifying agent according to sentence 9 of said paragraph. It is noted that the latter reading of this passage does not provide a basis for the emulsifying agent comprising both an ionic and a non-ionic detergent. In addition, the subject-matter according to claims 1 and 8 of auxiliary request VI is more specific in that the oil droplet emulsion claimed therein comprises the specific combination of a protein with an anionic and a non-ionic detergent.

In order to provide a basis for this combination, in particular in connection with the anionic detergent which is not disclosed on page 9, the appellant-proprietor also made reference to page 29 of the original application, which at the end of its first paragraph discloses an oil droplet emulsion comprising a protein and an anionic detergent. Nothing is said there about an additional non-ionic detergent. In addition, it is not clear whether said passage on page 29 is linked to the passage on page 9 mentioned above, as the description and in particular the passages in between relate to various alternative embodiments including, among others, microparticles with adsorbed macromolecules (see page 18, penultimate paragraph) submicron emulsions with ionic surfactants

(see page 25, third paragraph), microparticles (see page 25, last paragraph) and oil droplet emulsion (see page 29).

The board wishes to emphasise that amendments must be clearly and unambiguously disclosed in the original application. This is not the case when, as in the present case, the newly introduced features are taken from various places of a pool of unconnected or loosely connected pieces of information and formed to a new entity in the claim. As a consequence, the requirements of Article 123(2) EPC are not met.

6.2.2 Claim 2 in combination with claim 8

Claim 2 in combination with claim 8 discloses a microemulsion comprising a metabolizable oil, an emulsifying agent comprising a cationic detergent and a CpG oligonucleotide having adsorbent functionality. The reasoning submitted in point 6.2.1 above applies *mutatis mutandis* to the present case: adjuvant compositions comprising an oligonucleotide having at least one CpG motif are disclosed in the third sentence of the fifth paragraph on page 9 of the original application, microemulsions formulated with an ionic detergent are mentioned in the preceding sentence. For the same reasons as outlined in the second paragraph of point 6.2.1 above, page 9 of the original application does not provide a basis for the combination ionic detergent plus non-ionic detergent, the non-ionic detergents being disclosed further down in the ninth sentence of said fifth paragraph on page 9. For the same reasons as outlined in point 6.2.1, there is no clear link between pages 9 and 29, in which the

combination cationic detergent plus CpG oligonucleotide is disclosed. As a consequence, the subject-matter of claim 2 in combination with claim 8 does not meet the requirements of Article 123(2) EPC either.

7. Auxiliary request VII

7.1 Article 123(3) EPC

In view of the fact that the CpG oligonucleotides are now limited to compounds having adjuvant functionality, the requirements of Article 123(3) EPC are met (see point 6.2 above)

7.2 Article 123(2) EPC

The combination of claim 1 plus claim 7 of auxiliary request VII is identical to the combination of claim 2 plus claim 8 of auxiliary request VI. As a consequence, the requirements of Article 123(2) EPC are not met for the same reasons as outlined in point 6.2.2 above.

8. In view of this finding, an evaluation of the further objections raised by the appellant-opponent is not necessary.

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:

N. Maslin U. Oswald