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**Datasheet for the decision
of 16 December 2020**

Case Number: T 1627/18 - 3.3.07

Application Number: 11736500.7

Publication Number: 2590626

IPC: A61K9/127, A61K39/00, C12N15/86

Language of the proceedings: EN

Title of invention:
LIPOSOMES WITH LIPIDS HAVING AN ADVANTAGEOUS PKA-VALUE FOR RNA
DELIVERY

Patent Proprietor:
GlaxoSmithKline Biologicals SA

Opponent:
Dennemeyer & Associates S.A.

Headword:
Liposomes with lipids having an advantageous pKa-value for RNA
delivery / GLAXOSMITHKLINE

Relevant legal provisions:
EPC Art. 54(2), 100(a)
RPBA 2020 Art. 11, 12(2)
EPC R. 84(2)

Keyword:

Novelty - main request (yes)

Remittal - special reasons for remittal



Beschwerdekammern

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Case Number: T 1627/18 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 16 December 2020

Appellant: GlaxoSmithKline Biologicals SA
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 13 April 2018
revoking European patent No. 2590626 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairman D. Boulois
Members: E. Duval
P. Schmitz

Summary of Facts and Submissions

- I. European patent 2 590 626 ("the patent") was granted on the basis of 13 claims.

Claim 1 of the patent reads as follows:

"A liposome for *in vivo* delivery of RNA to a vertebrate cell, the liposome having a lipid bilayer encapsulating an aqueous core, wherein: (i) the lipid bilayer comprises a lipid having a pKa in the range of 5.0 to 6.8 when measured as described in the section "pKa measurement" of the description; and (ii) the aqueous core includes a RNA which encodes an immunogen."

- II. An opposition was filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application as filed.
- III. The appeal was filed by the patent proprietor (appellant) against the decision of the opposition division to revoke the patent.

The decision was based on the patent as granted as main request, and on auxiliary requests 1-11 filed with the letter dated 12 January 2018.

The following documents in particular were cited in the decision:

E1: WO98/10748

E9: WO2005/120152

IV. The opposition division decided that:

- (a) The ground for opposition under Article 100(c) EPC did not prejudice the maintainance of the patent as granted, i.e. according to the main request. However, the subject-matter of the main request lacked novelty over the disclosure of E9 as a whole.

In particular, the skilled person was directly pointed to passages of E9 directed to nucleic acids that encode an immunogen, which could be part of a DNA or RNA strand. The skilled person was also directly pointed to Example 4 of E9 because said example was concerned with stable nucleic acid lipid particles (SNALP) and showed that the cationic lipids DLinDMA, DLenDMA and DODMA exhibited the highest percentage of encapsulated nucleic acid. DLinDMA was a lipid according to claim 1. The selection of one out of two species of nucleic acids, namely DNA or RNA, and one out of three lipids (DLinDMA, LenDMA or DODMA) did not fall under the "two-lists principle" and led to subject-matter falling within the scope of claim 1. Hence E9 directly and unambiguously disclosed liposomes which comprised both a RNA which encodes an immunogen as bioactive agent and a lipid falling under the scope of claim 1.

- (b) None of the auxiliary requests was allowed by the opposition division:
 - (i) Auxiliary requests 2-6, 8, 10 and 11 were not admitted into the proceedings.

(ii) Auxiliary request 1, 7 and 9 were admitted into the proceedings, but were not considered to be allowable.

- V. With its statement of grounds of appeal filed on 23 August 2018, the appellant defended its case on the basis of the patent as granted as main request, and on the basis of auxiliary requests 1-9 filed by letter of 15 March 2017 and auxiliary requests 10 and 11 filed by letter of 12 January 2018, wherein corrected versions of auxiliary requests 2 and 10 were enclosed with the grounds of appeal.
- VI. The respondent (opponent) replied to the appellant's grounds of appeal.
- VII. The Board issued a communication pursuant to Article 15(1) RPBA. In this communication, the Board expressed the preliminary opinion that the subject-matter of the main request (i.e. the patent as granted) was novel over E9 and E1. The Board also indicated that, if the subject-matter of the main request was found to be novel, it intended to remit the case to the opposition division, under Article 11 RPBA 2020, for assessment of the essential issues which the appealed decision did not address.
- VIII. By letter dated 6 November 2020, the respondent withdrew its opposition against the patent.
- IX. After a communication of the Board, the appellant stated that it agreed to the case being remitted to the opposition division without oral proceedings. Therefore, the oral proceedings were cancelled.

X. The appellant's arguments can be summarised as follows:

- (a) The main request was novel over E9, because selections from many different lists were required to reach the subject-matter of claim 1.

In particular, E9 described the delivery of bioactive agents to a cell using liposomes comprising lipids of Formula I or II, which did not all fall within the scope of claim 1. Regarding the bioactive agents, E9 further described several lists including nucleic acid type, product-encoding versus silencing, therapeutic or diagnostic products, or gene-product type.

The opposition division's assertions that the skilled person was directly pointed from one paragraph to another, or was directly pointed to example 4 of E9 was unfounded. Example 4 related to liposomes encoding siRNA which was incapable of expressing an immunogen but was, instead, used for gene silencing.

Regarding auxiliary request 9, the opposition division had found its subject-matter to lack novelty over E1 but had not explained why E1 directly and unambiguously disclosed this claimed subject-matter. Selections from at least six lists were required to reach the claimed subject-matter, including the choice from RNA or DNA and the choice of a cationic lipid component.

XI. The appellant requests that the decision under appeal be set aside and that the patent be maintained as granted, or, in the alternative, on the basis of one of

the auxiliary requests 1-11 as defined in its grounds of appeal and as set out under V.

Furthermore, the appellant submits that the opposition division committed several procedural violations in relation with its decision not to admit auxiliary claim requests into the proceedings, and requests that this aspect of the decision be set aside.

Reasons for the Decision

1. Main request (patent as granted), novelty of claim 1

1.1 Claim 1 of the main request pertains to a liposome having a lipid bilayer encapsulating an aqueous core, characterised in particular in that:

(i) the lipid bilayer comprises a lipid having a pKa in the range of 5.0 to 6.8; and

(ii) the aqueous core includes a RNA which encodes an immunogen.

For the claimed invention to lack novelty, the combination of the above features must be directly and unambiguously derivable from the prior art.

1.2 Novelty over E9

1.2.1 With respect to feature (ii), the appealed decision refers to page 4, lines 4-8 and page 22 (line 22) to page 23 (line 24), in particular to page 23, lines 15-18, which mentions "a nucleic acid [that] encodes a polypeptide expressed in a subject [...] to generate an

immune response against the polypeptide expressed by the gene".

The Board finds that the choice of such a nucleic acid generating an immune response results from a selection from the host of active compounds or nucleic acids which, in the general disclosure of E9, may be encapsulated into the liposome. E9 generally considers bioactive agents such as antineoplastic agents, antibiotics, immunomodulators, anti-inflammatory agents, agents acting on the central nervous system, peptides, proteins and nucleic acids (such as DNA or RNA, including siRNA, see page 4, lines 4-8). Even in the context of nucleic acid lipid particles (SNALP), nucleic acids generating an immune response are only mentioned among numerous other alternative embodiments, without being identified as preferred (see page 22, line 22 to page 23, line 24). Additionally, RNA must be chosen as this nucleic acid to arrive at the claimed feature of a RNA which encodes an immunogen. Contrary to the opposition division's assertion, E9 does not contain any particular pointer to, or any examples of, a RNA encoding an immunogen.

- 1.2.2 As to feature (i), the passage cited in the appealed decision (namely example 4, including the table in paragraph [0211]) discloses SNALPs comprising DLinDMA, DLenDMA and DODMA as cationic lipids. However, the SNALPs of example 4 of E9 do not comprise a RNA which encodes an immunogen, but instead encapsulate siRNA, which is used for gene silencing. Beyond DLinDMA, DLenDMA and DODMA, E9 generally considers numerous lipids for the formation of liposomes (see the formula I and II in paragraphs [0006] and [0008], as well as the examples). Even if DLinDMA, DLenDMA and DODMA could be assumed to have a pKa in the range 5.0-6.8 in light

of paragraph [0010] of the patent, the same cannot be said for the other lipids considered in E9. No reason was put forward why the particular example 4 of E9 should express a general preference for these three individual cationic lipids beyond the context of siRNA.

1.2.3 The Board can also not discern in E9 a pointer to the combination of the cationic lipids of example 4 with the nucleic acid encoding an immunogen of page 23. In other words, the Board cannot find in E9 a disclosure of the above feature (ii) in combination with feature (i).

1.2.4 Thus the subject-matter of claim 1 of the main request is novel over E9.

1.3 Novelty over E1

1.3.1 The opposition division also found the narrower subject-matter of auxiliary request 9 to lack novelty over E1. Consequently, in the following, the Board assesses whether the subject-matter of the main request is novel over E1.

1.3.2 E1 discloses liposomes comprising an entrapped polynucleotide operatively coding for an immunogenic polypeptide (see claim 1 and page 5, lines 4-6). The polynucleotide may be DNA or RNA (see claims 2-4). DC-Chol is cited among the lipids of E1.

It was debated during the proceedings whether DC-Chol is a lipid as defined in claim 1, having a pKa in the range 5.0-6.8. The Board however finds that the claimed subject-matter is anyway novel over E1, because E1 does not disclose a liposome comprising, in combination, DC-Chol and RNA.

- 1.3.3 DC-Chol is mentioned among the various lipids that can be used in E1 (see claim 11), without being singled out as being preferred over the other lipids. Additionally, even though RNA appears in a list of only 2 alternatives (see E1, claims 2 and 4), E1 explicitly states that the RNA alternative is least preferred (see page 6, lines 24-28). In these circumstances, and in the absence of a pointer to this combination, the Board comes to the conclusion that E1 does not provide a direct and unambiguous disclosure of a liposome comprising both RNA and DC-Chol.
- 1.3.4 Thus the subject-matter of claim 1 of the main request is also novel over E1.

2. Admittance of the auxiliary requests

The opposition division decided not to admit auxiliary requests 2-6, 8, 10 and 11 into the proceedings. The appellant requests that this aspect of the decision be set aside, because the opposition division committed several procedural violations in doing so.

The Board shares the appellant's opinion that the opposition division committed a procedural violation by not admitting these requests, for the reasons set out in the communication under Article 15(1) RPBA dated 28 October 2020 (point 1.). However, since the appealed decision can be set aside on the basis of the main request, the auxiliary requests need not be considered further.

2.1 Remittal to the opposition division

The sole reason in the appealed decision for rejecting the main request is a lack of novelty. It follows from the reasoning above that this finding of lack of novelty must be set aside.

Since the opposition was withdrawn, the question arises as to whether the opposition proceedings should be continued pursuant to Rule 84(2) EPC for assessment of the grounds of opposition under Article 100(a) EPC (inventive step) and 100(b) EPC, which have not been considered so far by the opposition division.

The primary object of the appeal proceedings is to review the decision under appeal in a judicial manner (see Article 12(2) RPBA 2020). In the present case, no decision exists for these outstanding issues. The Board considers that these circumstances constitute special reasons in the sense of Article 11 RPBA 2020 for remitting the case to the opposition division, in accordance with the appellant's request. Upon remittal, the opposition division will have to exercise its discretion as to whether the opposition proceedings should be continued pursuant to Rule 84(2) EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the opposition division for further prosecution.

The Registrar:

The Chairman:



B. Atienza Vivancos

D. Boulois

Decision electronically authenticated