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**Datasheet for the decision
of 22 March 2017**

Case Number: T 2228/13 - 3.3.07
Application Number: 07723327.8
Publication Number: 2004141
IPC: A61K9/127, A61K48/00, C12N15/88
Language of the proceedings: EN

Title of invention:

AN EFFICIENT METHOD FOR LOADING AMPHOTERIC LIPOSOMES WITH
NUCLEIC ACID ACTIVE SUBSTANCES

Applicant:

Marina Biotech, Inc.

Headword:

AN EFFICIENT METHOD FOR LOADING AMPHOTERIC LIPOSOMES WITH
NUCLEIC ACID ACTIVE SUBSTANCES/Marina Biotech, Inc.

Relevant legal provisions:

EPC Art. 123(2), 84

Keyword:

Main request - Amendments (Yes)
Main request - Clarity (Yes)

Decisions cited:

Catchword:



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Case Number: T 2228/13 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 22 March 2017

Appellant: Marina Biotech, Inc.
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Representative: Srinivasan, Ravi Chandran
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 2 May 2013
refusing European patent application No.
07723327.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman A. Uselli
Members: D. Boulois
I. Beckedorf

Summary of Facts and Submissions

- I. The appeal lies from the decision of the examining division to refuse European patent application n° 07 723 327.8. The decision was based on the set of claims filed with letter of 7 July 2011 as main request.

Claim 1 of the main request read as follows:

"1. A method for preparing amphoteric liposomes loaded with a nucleic acid active substance as cargo, characterised by providing an aqueous solution of said nucleic acid active substance and an alcoholic lipid mixture wherein adjustment of at least one of said solutions to an acidic pH is required; and admixing said solutions wherein the amphoteric liposomes form via suspension at said acidic pH, and wherein the amphoteric liposomes encapsulate said nucleic acid active substance; and thereafter elevating the pH of the suspension to pH 7 or more or elevating the ionic strength of the suspension, wherein said amphoteric liposomes have a cationic charge at pH 7.5 and a cationic charge at pH 4."

- II. According to the decision under appeal, some amendments in claims 1 and 19-22 introduced subject-matter which extended beyond the content of the application as filed, contrary to Article 123(2) EPC. The amendments in claim 1 were the following :
- the feature "wherein said amphoteric liposomes have an anionic charge at pH 7.5 and a cationic charge at pH 4" had no basis in the application as filed;
 - the feature "polyanionic" had been suppressed;
 - the features "under conditions such that said liposomes form aggregates, and thereafter treating said

suspension to dissociate said aggregates" had been removed without any apparent basis.

The application did not meet the requirements of Article 84 EPC, since claim 22 referred to "a process as claimed in claims 1-20", while claims 19 and 20 did not relate to a process. Also, the wording was such that claim 22 could not be seen as being dependent on claim 19. The present claim set therefore also contained two independent product claims, namely claims 19 and 22, contrary to Rule 43(2) EPC.

Dependent claims 2 and 24 defined the invention in relation to an unclear feature, namely the isoelectric point of the lipid mixture solution and of the liposomes, respectively.

The application therefore did not meet the requirements of Article 84 EPC.

- III. The applicant (hereafter called appellant) filed an appeal against said decision.
- IV. With the statement of grounds of appeal dated 11 September 2013 the appellant submitted a main request.
- V. A communication expressing the board's preliminary opinion of the board dated 23 December 2016 was sent to the applicant.
The Board's opinion was that the main request did not meet the requirements of Article 123(2) and 84 EPC.
- VI. With a letter dated 12 January 2017, a new main request was submitted.

VII. In a phone conversation held on 1 February 2017, the rapporteur informed the applicant about some deficiencies in dependent claims 5, 7 and 15.

VIII. With a letter dated 1 February 2017, the appellant submitted a new main request and auxiliary request 1.

Claim 1 of the main request read as follows:

"1. A method for preparing amphoteric liposomes loaded with a polyanionic nucleic acid active agent as cargo, comprising providing an aqueous solution of the polyanionic nucleic acid active agent, and a solution of a lipid mixture in a water-miscible alcohol solvent, wherein at least one of the aqueous nucleic acid solution and alcoholic lipid mixture solution is adjusted to an acidic pH, mixing defined quantities of the aqueous nucleic acid solution and the alcoholic lipid solution by injecting the alcoholic solution of lipid mixture into the aqueous solution of the polyanionic nucleic acid active agent or vice versa, or by combining two metered separate streams of provided lipid solution and nucleic acid solutions, to form a suspension of amphoteric liposomes, wherein the concentration of the water-miscible alcohol solvent in the suspension is greater than 20% by volume; diluting said suspension with additional aqueous media such that the alcohol content is less than 20% by volume; and dissipating interaction between the amphoteric liposomes and the polyanionic nucleic acid active substance by increasing the pH value to greater than 7 and/or by increasing the ionic strength."

The remaining claims of the main request were dependent on claim 1.

- IX. The appellant's written arguments can be summarised as follows:

Claim 1 now specifies a dilution step which finds a basis at page 7, lines 9 to 12 of the description. Dependent claim 14 has been deleted as well as the product claims.

- X. Requests

The appellant essentially requests that the decision under appeal be set aside and that the main request or auxiliary request 1 submitted with letter of 1 February 2017 be found to meet the requirements of Articles 84 and 123(2) EPC, and that the case be remitted to the examining division for consideration of novelty and inventive step.

Reasons for the Decision

1. The decision is taken in the written proceedings since the appellant requested oral proceedings only in the event that the Board did not allow the appellant's request of remitting the case to the examining division on the basis of the main request or auxiliary request 1.
2. Main request - Article 123(2) EPC

The subject-matter claimed in the main request has been deeply modified in comparison to the main request which

was the subject of the decision of the examining division.

The following features have been added to claim 1:

- i) providing an aqueous solution of the polyanionic nucleic acid active agent, and a solution of a lipid mixture in a water-miscible alcohol solvent, wherein at least one of the aqueous nucleic acid solution and alcoholic lipid mixture solution is adjusted to an acidic pH,
- ii) mixing defined quantities of the aqueous nucleic acid solution and the alcoholic lipid solution by injecting the alcoholic solution of lipid mixture into the aqueous solution of the polyanionic nucleic acid active agent or vice versa, or by combining two metered separate streams of provided lipid solution and nucleic acid solutions, to form a suspension of amphoteric liposomes, wherein the concentration of the water-miscible alcohol solvent in the suspension is greater than 20% by volume;
- iii) diluting said suspension with additional aqueous media such that the alcohol content is less than 20% by volume; and
- iv) dissipating interaction between the amphoteric liposomes and the polyanionic nucleic acid active substance by increasing the pH value to greater than 7 and/or by increasing the ionic strength.

Feature i) is disclosed on page 25, lines 25 to page 26, line 3 of the original description (see WO 2007/107304, identical to the application as filed). Steps ii) and iii) are disclosed on page 26 lines 5-10 and further on page 7, lines 4-14, and step iv) can be found on page 26, lines 14-17.

As regards the amended dependent claims, the basis was as following:

Claim	Basis in the application as filed
2	page 29, lines 10-11
3	original claim 3
4	original claim 4
5	original claim 8
6	page 7, lines 4-14
7	original claim 9
8	original claim 12
9	original claim 13
10	page 8, lines 1-2
11	page 26, lines 31-32
12	original claim 21
13	original claim 26
14	original claim 21

The subject-matter of the claims of the main request is therefore directly and unambiguously derivable from the application as originally filed, and this request meets the requirements of Article 123(2) EPC.

3. Main request - Article 84 EPC

All features objected by the Examining Division in its decision has been deleted in the claims of the main requests and the amended features do not introduce any unclarity to the claims.

Consequently, the main request meets the requirements of Article 84 EPC.

4. Remittal to the examining division

Although Article 111(1) EPC does not guarantee a party an absolute right to have all the issues in the case considered by two instances, it is well recognised that any party should, whenever possible, be given the opportunity to said consideration by two instances of the important elements of the case. The essential function of an appeal proceedings is to consider whether the decision which has been issued by the first instance department is correct. Hence, a case is normally remitted if further requirements for patentability have not yet been examined and decided by the department of first instance. This is the situation here, since at least novelty and inventive step are not part of the decision of the first instance.

Hence, the Board considers it appropriate to remit the case to the Examining Division for further prosecution on the basis of the main request.

Order

For these reasons it is decided that:

1. The decision is set aside.
2. The case is remitted to the examining division on the basis of the main request for further prosecution.

The Registrar:

The Chairman:



S. Fabiani

A. Usuelli

Decision electronically authenticated