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**Datasheet for the decision
of 9 October 2012**

Case Number: T 1841/08 - 3.3.02

Application Number: 01927169.1

Publication Number: 1282403

IPC: A61K 9/127

Language of the proceedings: EN

Title of invention:

Non-invasive gene targeting to the brain

Applicant:

The Regents of The University of California

Opponent:

-

Headword:

-

Relevant legal provisions:

EPC Art. 83

EPC R. 137(3)

RPBA Art. 12, 15

Keyword:

"Main request: Sufficiency of disclosure (no)"

"Auxiliary requests: Admissibility (no)"

Decisions cited:

-

Catchword:

-



Case Number: T 1841/08 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 9 October 2012

Appellant: The Regents of The University of California
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 2 May 2008
refusing European patent application
No. 01927169.1 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
R. Cramer

Summary of Facts and Submissions

- I. European patent application No. 01 927 169.1, based on PCT/US2001/012599 and published as WO 2001/082900, was refused by a decision of the examining division on the basis of Article 97(2) EPC.

The wording of claim 1 of the set of claims of the main request before the examining division reads:

"A receptor-specific liposome for delivering a gene across the blood brain barrier and the brain cell membrane,

the liposome having an exterior surface and an internal compartment, the exterior surface defining a sphere having a diameter less than 200nm,

the liposome comprising:

a therapeutic gene at least 100 nucleotides in length located within a plasmid and located within the internal compartment of the liposome;

a plurality of blood brain barrier and brain cell membrane targeting agents; and

a plurality of conjugation agents wherein each of the targeting agents is connected to the exterior surface of the liposome via at least one of the conjugation agents."

- II. The examining division considered that the teaching as defined in claim 1 was not sufficiently disclosed because the application did not describe how to

encapsulate a gene in the internal compartment of a liposome without the use of a cationic lipid, indicated as being necessary in the description and the submissions of the appellant, there being no reference to a content of cationic lipid in the claim. Consequently, the skilled person would not be able to carry out the invention over the whole claimed scope.

Again with regard to the missing feature of a content of cationic lipid, the examining division concluded that the application did not meet the requirements of Article 84 EPC in connection with Rules 43(1) and (3) EPC.

In addition, the division held that the teaching of claim 1 of the main request and as a consequence also that of independent claims 10 and 12 was not inventive (Article 56 EPC).

III. The appellant lodged an appeal against the decision of the examining division and filed grounds of appeal together with four sets of claims as main and auxiliary requests.

Claim 1 of the main request is unamended with respect to claim 1 before the examining division.

The text of claim 1 of the first auxiliary request differs from claim 1 as decided by the examining division in the passage between "... comprising:" and "a plurality ...", which defines the position of the contained gene. The passage contained in the main request is replaced by

"a plasmid containing a therapeutic gene at least 100 nucleotides in length, said plasmid located within the internal compartment of the liposome;".

The text of claim 1 of the second auxiliary request is identical to the text of claim 1 of the main request with the additional passage "a cationic lipid" added after "... comprising:".

Claim 1 of the third auxiliary request contains both amendments of the other auxiliary requests.

IV. As an annex to the statement of grounds of appeal, a declaration of the inventor was filed:

(10) Statutory declaration of Mr Pardridge of 28 August 2008 filed in the original with letter of 5 September 2008

In this declaration, the following evidence was cited (filed with the statement of grounds of appeal):

(11) Gregoriadis et al; "High yield incorporation of plasmid DNA within liposomes: effect on DNA integrity and transfection efficiency", Journal of Drug Targeting, Vol. 3, 1996, 469-475

V. With letter of 23 August 2012 the appellant indicated that it would not attend the oral proceedings set for 9 October 2012 and that it wished a decision on the basis of the documents on file.

The oral proceedings took place in the absence of the appellant.

- VI. The appellant's arguments in the written procedure with respect to Article 83 EPC can be summarised as follows:

The presence of a cationic lipid was not an essential feature of the invention because there were several general statements in the application that the character of the invention was "not limited to particular cationic liposomes". The alternatives were partly no liposomes at all but nanocontainers in general (see in particular document (10)). Moreover, it was set out that the use of cationic lipids was just "one way" to achieve the goals of the invention.

In addition, there was evidence that the use of a cationic lipid was not generally compulsory in the art of incorporation of plasmid DNA, even within liposomes (document (11)).

- VII. The appellant (applicant) requested with the grounds of appeal that the decision under appeal be set aside and oral proceedings be held; further, the appellant requested in its letter of 23 August 2012 that a decision be issued on the basis of the documents on file.

The board concluded that the appellant implicitly requested that a patent be granted on the basis of the main request or one of the three auxiliary requests filed with the grounds of appeal.

Reasons for the Decision

1. The appeal is admissible.

2. *Main request; Article 83 EPC*

2.1 According to the application as originally filed

"Suitable types of liposomes are made with neutral phospholipids such as 1-palmitoyl-2-oleoyl-sn-glycerol-3-phospho-choline (POPC), diphosphatidy phosphocholine, distearoylphosphatidylethanolamine (DSPE), or cholesterol, **along with a small amount (1%) of cationic lipid**, such as didodecyldimethylammonium bromide (DDAB) **to stabilize the anionic DNA within the liposome.**"

(page 6, lines 13 to 18; emphasis by the board)

In view of this text together with the examples of the application, both relating to liposomes exclusively as does claim 1 of the main request, the board has no reason to depart from the conclusion of the examining division and the reasoning under Article 83 EPC in the impugned decision:

In the cited passage on page 6 of the application as originally filed it is stated that stabilisation of the anionic DNA within the liposome is necessary and that a cationic lipid, such as didodecyldimethylammonium bromide (DDAB) can be used to achieve that. In the examples (see in particular page 10, line 30 of the application under the heading "Pegylated Liposome synthesis and plasmid DNA encapsulation") nothing else is realised: The liposomes that are used in the experiments comprise DDAB.

Nevertheless, since the feature "content of a cationic lipid" is missing, claim 1 of the main request relates also to receptor-specific liposomes not containing a "cationic lipid" without any teaching being provided by the application on how the stabilisation could be achieved in these cases.

Consequently, the board considers it to be an undue burden on the person skilled in the art to find out what other conditions could lead to results equal to those that can be achieved by use of the "cationic lipid".

Therefore, the provisions of Article 83 EPC are not met.

2.2 The missing feature of a content of cationic lipid just hinders the skilled person from carrying out the claimed teaching and in fact relates to Article 83 EPC. On the other hand, even being challenged by the examining division as being in breach of Article 84 EPC because of this missing feature, claim 1 of the main request at least is not unclear in a manner that the skilled person could not recognise the matter for which protection is sought. For this reason, the application in suit, with respect to the subject-matter of this claim, can be assessed as to the requirements of Article 83 EPC without any difficulties.

2.3 Under these circumstances, namely claim 1 of the main request and the application not meeting the requirements of Article 83 EPC even taking account of Article 84 EPC, which are provisions of the EPC to be considered before addressing novelty and inventive step,

there is no need to comment on the issue in relation to Article 56 EPC.

3. *Auxiliary requests; admissibility*

3.1 As in any case of new requests, their admissibility has first to be examined.

The applicant did not file any auxiliary request in the proceedings before the examining division, although the examining division repeatedly pointed out deficiencies and why they had not been overcome by amendments filed by the applicant so far. With the statement of grounds of appeal the applicant filed for the first time auxiliary requests in addition to the main request, the main request being identical to the last set of claims before the examining division. The applicant did not give any grounds why these requests were filed for the first time in appeal proceedings, and to what extent they would overcome the reasons for refusal in the decision under appeal as required by Article 12(2) of the Rules of Procedure of the Boards of Appeal (RPBA).

As the auxiliary requests had not been filed before the examining division, admitting these requests into the appeal proceedings would mean that the board would have to examine them for the first time in appeal proceedings, or refer the matter back to the examining division. The main function of appeal proceedings is, however, to give a judicial decision upon the correctness of an earlier decision taken by a department of first instance. New requests may be admitted if they are serious attempts at overcoming objections. If they are not, the board has the

discretion not to admit them into the appeal proceedings (Rule 137(3) EPC and Article 12(4) RPBA).

As the applicant chose not to be present at oral proceedings, the board had no opportunity to ask the applicant why it believed that the auxiliary requests should be admitted. In view of Article 15(3) RPBA there was however no reason for the board to delay a decision on admissibility of the auxiliary requests as the applicant should have been aware that this issue would be addressed at oral proceedings as a matter of course.

When considering whether new requests are to be admitted into appeal proceedings, the following criteria are relevant:

- whether the new requests are an answer to the reasoning set out in the impugned decision and
- whether the amendments *prima facie* could solve the indicated problems

In the present case, the following special circumstances apply with regard to these criteria:

- Since in the first auxiliary request, there is only another wording to make clear that the therapeutic gene is contained within a plasmid, the reasoning and the conclusions of the examining division and the board relating to Article 83 EPC with respect to claim 1 of the main request - not depending on this feature - apply *mutatis mutandis* also to claim 1 of the first auxiliary request.

- The second and third auxiliary requests contain a feature that the requested liposomes comprise "a cationic lipid" without any further definition. This feature had already been introduced resulting in the set of claims filed with fax of 7 February 2008; the examining division's response is to be found in the minutes to a consultation by telephone dated 20 February 2008. The response was that such a request did not comply with Article 123(2) EPC.

In the statement of grounds, the appellant refers to the same source for original disclosure of the feature as was discussed with the examining division (page 6, line 17 of the application as originally filed) with no additional argument mentioned.

Moreover, the examining division proposed a draft of a claim (see minutes of a consultation by telephone dated 14 March 2008) consequently assumed to be free of this deficiency. Despite this, claims 1 of the present second and third auxiliary requests differ from the proposal in this feature. The examining division suggested the wording "... and a small amount of cationic lipid ..." while in claims 1 of the second and the third auxiliary requests "small amount" is missing without any explanation.

As a consequence, the indicated criteria relating to the assessment of admissibility of the requests are not met.

- 3.2 In view of these considerations, the board exercises its discretion under Rule 137(3) EPC and

Article 12(4) RPBA and the auxiliary requests are not admitted into the proceedings.

- 3.3 Under these circumstances, the additional arguments of the appellant cannot succeed either.

Its argument that the overall disclosure of the application as originally filed mentioned nanocontainers - meaning an even broader subject-matter than the receptor-specific liposomes defined in claim 1 of the main request - just illustrates and emphasises the problem of establishing the special conditions enabling the person skilled in the art to put the teaching into practice.

In addition, it does not matter that alternative methods of incorporating plasmid DNA within liposomes, not based on cationic lipids, are described somewhere in the literature (document (11) as cited by the inventor in its declaration). This literature was not part of the application as originally filed. Moreover, all statements in the application supporting a specific teaching to enable the skilled person to carry it out are directed to the use of a cationic lipid, and, as a single citation, document (11) also cannot be found to represent the common general knowledge of the person skilled in the art.

4. Consequently, the subject-matter of the application in the form of claim 1 of the main request is not sufficiently disclosed (Article 83 EPC) and the auxiliary requests are not admitted into the proceedings.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

N. Maslin

U. Oswald