

**Internal distribution code:**

- (A)  Publication in OJ  
(B)  To Chairmen and Members  
(C)  To Chairmen  
(D)  No distribution

**Datasheet for the decision  
of 17 February 2010**

**Case Number:** T 0290/05 - 3.3.02

**Application Number:** 98958234.1

**Publication Number:** 1039880

**IPC:** A61K 9/127

**Language of the proceedings:** EN

**Title of invention:**

Method for developing, testing and using associates of macromolecules and complex aggregates for improved payload and controllable de/association rates

**Applicant:**

IDEA AG

**Opponent:**

-

**Headword:**

Associates of Macromolecules and Complex Aggregates/IDEA AG

**Relevant legal provisions:**

EPC Art. 84

EPC R. 103

**Relevant legal provisions (EPC 1973):**

-

**Keyword:**

"All requests: Article 84 - (no): lack of clarity and undue burden"

"No reimbursement of the appeal fee"

**Decisions cited:**

-

**Catchword:**

-



Case Number: T 0290/05 - 3.3.02

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.02  
of 17 February 2010

**Appellant:**

IDEA AG  
Frankfurter Ring 193a  
D-80807 München (DE)

**Representative:**

Maiwald, Walter  
Maiwald Patentanwalts GmbH  
Elisenhof  
Elisenstrasse 3  
D-80335 München (DE)

**Decision under appeal:**

Decision of the Examining Division of the  
European Patent Office posted 25 October 2004  
refusing European application No. 98958234.1  
pursuant to Article 97(1) EPC 1973.

**Composition of the Board:**

**Chairman:** U. Oswald  
**Members:** A. Lindner  
J. Van Moer

## Summary of Facts and Submissions

I. European patent application No. 98 958 234.1 was refused by a decision of the examining division posted on 25 October 2004 on the basis of Article 97 EPC on the grounds that the subject-matter of the main and sole request lacked clarity and conciseness, lacked novelty and related to methods of therapeutic treatment of the human or animal body.

II. The decision was based on claims 1-67 of the main and sole request filed with letter of 28 June 2002. The independent claims read as follows:

"1. A combination of at least one first and at least one second substance having amphipatic properties in a suitable liquid medium, and at least one third substance, for optimising and controlling the association of said at least one third substance to extended surfaces, especially membrane surfaces, formed by said at least one first and said at least one second substance in contact with said liquid medium, characterised in that

- said at least one first and said at least one second substances have different solubilities in said liquid medium,
- said at least one first substance is selected from the group containing lipids or lipid-like materials, or a combination thereof, and is less soluble in said liquid medium than said at least one second substance and forms aggregates having extended surfaces,
- said at least one second substance is selected from the group containing edge-active substances,

surfactants, or mixtures thereof, and is more soluble in said liquid medium than said at least one first substance and forms smaller aggregates than said at least one first substance,

- said at least one third substance is one or several chain molecules, and has an increased association with said extended surfaces formed by said at least one first substance and said at least one second substance than with extended surfaces formed by said at least one first substance or at least one second substance alone.

49. A method of preparing a combination according to any one of claims 1 to 48 in the form of a formulation of a biologically, cosmetically and/or pharmaceutically active agent, characterised by the steps of

- selecting the at least one first and the at least one second substance, such that said extended surfaces formed by said at least one first and said at least one second substance attract and associate to a greater extent with said at least one third substance acting as active agent than the surfaces formed by the at least one first substance alone;
- generating said combination of surface-forming at least one first and at least one second substances by means of controlled mechanical fragmentation, in the presence of or before being mixed with the at least one third substance in the form of said agent molecules, such that said at least one third substance associates with said extended surface formed by controlled mechanical fragmentation.

63. Use of a combination of substances according to any one of claims 1 to 48 for the manufacture of drug

carriers, drug depots, or for any other kind of medicinal or biological application forms.

64. Use of a combination of substances according to any one of claims 1 to 48 for the manufacture of a formulation for the use in bioengineering or for genetic manipulations.

65. Use of a combination of substances according to any one of claims 1 to 48 for the manufacture of a formulation for the use in separation technology, for (bio)processing or for diagnostic purposes.

66. Use of a combination of substances according to any one of claims 1 to 48 to stabilise surface-associating molecules, especially chain molecules, that are at least partially amphipatic, such as (derivatised) proteins, polypeptides, polynucleotides, or polysaccharides and/or in catalysing processes which involve such molecules in the surface-associated state.

67. Use of a combination of substances according to any one of claims 1 to 48 to affect the kinetics and/or the reversibility of association or dissociation between said surface-associating molecules and a complex, adaptable surface, whereby the higher surface charge density and/or greater surface softness and/or surface defect density speeds up the association, or the corresponding reduction slows down the rate of association or else induces partial molecular dissociation."

III. The documents cited during the examination and appeal proceedings included the following:

- (1) CA-A-2 052 164
- (2) WO 92/03122
- (3) WO 98/17255

IV. The arguments in the decision may be summarised as follows:

As regards the requirements of Article 84 EPC, it was reasoned that the functional features in independent claims 1 and 49 rendered the claimed subject-matter unclear. Moreover, they put an undue burden on the skilled person trying to put the invention into practice. In connection with novelty, it was held that the subject-matter of independent claims 1 and 49 was anticipated by documents (1) to (3). Moreover, the subject-matter of claims 63, 64 and 65 included methods of treatment of the human or animal body.

V. The appellant (applicant) lodged an appeal against this decision.

VI. With the statement of the grounds of appeal dated 22 February 2005, the appellant filed a new main request and auxiliary requests 1 to 3. The independent claims 1 of each request read as follows:

*(a) Main request:*

"1. A combination of at least one first and at least one second substance having amphipatic properties in a suitable liquid medium, and at least one third

substance, for optimising and controlling the association of said at least one third substance to extended surfaces, especially membrane surfaces, formed by said at least one first and said at least one second substance in contact with said liquid medium, characterised in that

- said at least one first and said at least one second substances have different solubilities in said liquid medium,
- said at least one first substance is selected from the group containing lipids or lipid-like materials, or a combination thereof, and is less soluble in said liquid medium than said at least one second substance and forms aggregates having extended surfaces,
- said at least one second substance is selected from the group containing edge-active substances, surfactants, or mixtures thereof, and is more soluble in said liquid medium than said at least one first substance and forms smaller aggregates than said at least one first substance,
- said at least one third substance is one or several chain molecules, and has an increased association with said extended surfaces formed by said at least one first substance and said at least one second substance than with extended surfaces formed by said at least one first substance or at least one second substance alone."

*(b) Auxiliary request 1:*

"1. A combination of substances in a liquid medium, comprising

- at least one first surface-forming amphipathic substance selected from lipids or lipid-like materials,
- at least one second surface-destabilising amphipathic substance, which is more soluble in said liquid medium than said first substance, and is selected from surface-active substances or surfactants,

characterised in that said combination forms extended surfaces in contact with said liquid medium, with which surfaces the molecules of a third amphipathic substance, selected from chain molecules or macromolecules, associate."

*(c) Auxiliary request 2:*

"1. A combination of substances in a liquid medium, comprising

- at least one first surface-forming amphipathic substance selected from lipids or lipid-like materials,
- at least one second surface-destabilising amphipathic substance, which is more soluble in said liquid medium than said first substance, and is selected from surface-active substances or surfactants, wherein said combination forms extended surfaces in contact with said liquid medium, with which surfaces the molecules of a third amphipathic substance selected from chain molecules or macromolecules associate, characterised in that the

- extended surfaces with which the third substance is associated is obtainable by the steps of
- selecting the at least one first and the at least one second substance;
  - generating said combination of surface-forming at least one first and surface-destabilising at least one second substance by means of controlled mechanical fragmentation selected from filtration, pressure change or mechanical homogenisation, shaking, stirring, or mixing in the presence of the at least one third substance in the form of said agent molecules, or by first preparing the surface by steps including sequential mixing, and subsequent addition of the associating molecules;
  - allowing the molecules of the third substance to associate with the extended surfaces formed by the combination, if necessary assisted by agitation, mixing or incubation, provided that such treatment does not break up the preformed surfaces."

*(d) Auxiliary request 3:*

- "1. Use of a combination of substances forming extended surfaces in contact with a liquid medium for the association of a third substance with said extended surfaces, wherein the combination comprises
- at least one first surface-forming amphipathic substance selected from lipids or lipid-like materials,
  - at least one second surface-destabilising amphipathic substance, which is more soluble in said liquid medium than said first substance, and is selected from surface-active substances or surfactants, and

wherein the third substance is amphipathic and selected from chain molecules or macromolecules."

- VII. By official communication of 24 September 2009, the appellant was invited to oral proceedings.
- VIII. With letter of 30 November 2009, the appellant withdrew his request for oral proceedings and requested a decision on the state of the file.
- IX. By fax of 30 November 2009, the oral proceedings were cancelled.
- X. The appellant's arguments with regard to the requirements of Article 84 EPC can be summarised as follows:

The functional claim language was justified and did not cause any unclarity. The present invention related to a combination of two substances forming extended surfaces with which a third substance associated. The improved association of the third substance with an extended surface formed by a surface-forming substance and a surface-destabilising substance as compared to an extended surface formed by a surface-forming substance alone constituted the distinguishing feature of the claimed subject-matter. The present invention could be carried out with a huge number of combinations of substances, provided that the functional definitions were respected. This was illustrated by 158 examples and 12 figures which provided sufficient information of how to rework the present invention. The present invention related to certain combinations, the components of which must have certain properties

relative to each other. As a consequence, these relative properties - e.g. component A is more soluble in the same liquid medium than component B - were essential for properly defining the invention. There was no better way of defining the present invention. On the contrary: a definition without these relative properties and restricted to specific substances would be unclear, as in that case the invention could not be carried out over the entire scope of the claim if these substances did not fulfil the criteria concerning the different solubilities in a given liquid medium.

As regards the alleged procedural violations committed by the examining division, the appellant argued that the application had been refused after a single official communication, although the complex subject-matter and detailed arguments given in the reply to said official communication would have required a second office action such as a further communication, an interview or oral proceedings. Moreover, the decision of the examining division contained an almost exact repetition of the objections raised in the single official communication. No comments were made in respect of the applicant's arguments or amendments. Only once did the examining division react to the applicant's arguments by citing a new text passage in the prior art on which the applicant had been unable to comment. Finally, the contested decision was contradictory in that, although it was stated that certain allegedly unclear features would not be taken into consideration, these features were nevertheless discussed in the evaluation of novelty.

XI. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request or, alternatively, on the basis of auxiliary request 1, 2 or 3, all filed with the statement of the grounds of appeal dated 22 February 2005. Moreover, reimbursement of the appeal fee was requested.

### **Reasons for the decision**

1. The appeal is admissible.

2. *Article 84 EPC*

2.1 Main request

2.1.1 Claim 1

Under Article 84 EPC the claim(s) shall define the matter for which protection is sought. They shall be clear and concise and be supported by the description. Accordingly, the question to be answered with respect to clarity under Article 84 EPC *inter alia* is whether it is possible to determine whether or not an embodiment falls within the scope of the claims or not. If so, the next question is whether such determination can be carried out with reasonable effort or whether it requires an undue burden for the skilled person.

In the present case, three different substances have to be selected from very large pools of compounds in a first step. Thus, the first substance has to be chosen from the group containing lipids and lipid-like

materials. The lipids are defined on page 9, lines 22-23 of the original application and include "any substance with characteristics similar to those of fats". This very vaguely defined group of compounds is further supplemented by the "lipid-like materials". This term is not clear, because there is no information whether this likeness concerns similarity in terms of molecular structure, physical or chemical properties or any other parameters. For that reason alone, the subject-matter of claim 1 is not clear.

The second substance is selected from the group containing edge-active substances, surfactants and mixtures thereof, which also comprises an infinite number of compounds.

The same goes for the third substance, which is selected from chain molecules.

Then, the skilled person, who is already at a loss to determine which compounds are included in the definition of lipid-like substances, must further examine whether the combination of the three substances, which comprises an infinite number of possibilities, fulfils the functional properties defined in the claims. Thus, it has to be tested among other things whether the first substance is less soluble in a given liquid medium than the second substance, whether the combination of the first and second substances forms aggregates having extended surfaces in said liquid medium and finally whether the third substance associates to the extended surfaces formed from the first and second substances. The series of tests described above requires considerable effort, which, as

was correctly pointed out by the examining division, amounts to an undue burden.

The appellant argued that it was not possible to define the invention more precisely without unduly restricting the scope of the claimed subject-matter and made reference to the numerous examples and the figures associated therewith, which allegedly demonstrated the wide variety of possible embodiments.

The board cannot agree with this line of argument: although the contested application comprises 158 examples, there are only very little variations in the composition of the products. Thus, in each of the 158 examples, phosphatidylcholine from soy-bean is used as lipid (first substance), a protein (insulin, interferon, IL-2, calcitonin or IgG) as the third substance and a phosphate buffer as liquid. Moreover, the selection of the surface-active agent (second substance) is limited to Na-cholate and Tween 80<sup>R</sup>. Therefore, the numerous examples do not justify the functional claim language; they do not demonstrate the impossibility of defining the invention in a more concrete way without unduly restricting the scope of the claims. As a consequence, the subject-matter of claim 1 does not meet the requirements of Article 84 EPC.

- 2.1.2 In view of this finding, an evaluation of the clarity of the further independent claims is not necessary.

2.2 Auxiliary request 1

2.2.1 Claim 1

The above evaluation concerning lack of clarity (see point 2.1.1 above) applies *mutatis mutandis* to claim 1 of auxiliary request 1: again, the skilled person is at loss to determine which substances are included in the lipid-like materials, and again all tests described in paragraph 2.1.1 above have to be carried out in order to find out whether a given composition is or is not included in claim. As a consequence, the subject-matter of claim 1 of auxiliary request 1 does not meet the requirements of Article 84 EPC either.

2.2.2 In view of this finding, an evaluation of the clarity of the further independent claims is not necessary.

2.3 Auxiliary request 2

2.3.1. Claim 1

Claim 1 of auxiliary request 2 is the same as claim 1 of auxiliary request 1 except that the claimed composition is now further characterised by the method of its preparation. However, the addition of the method of preparation does not overcome the objections raised above in connection with Article 84 EPC: the skilled person still does not know which substances are included in the term "lipid-like material" and he still has to carry out all the tests described in point 2.1.1 above in order to determine whether or not a given composition is encompassed by the claim. As a consequence, the subject-matter of claim 1 of auxiliary

request 2 does not meet the requirements of Article 84 EPC either.

2.3.2 In view of this finding, an evaluation of the clarity of the further independent claims is not necessary.

2.4 Auxiliary request 3

2.4.1 Claim 1

Claim 1 of auxiliary request 3 is the same as claim 1 of auxiliary request 1 except that the claim category has been changed from "product claim" to "use claim". This change of category can, however, not overcome the objections raised above in points 2.1.1 and 2.2.1. As a consequence, the subject-matter of claim 1 of auxiliary request 3 does not meet the requirements of Article 84 EPC either.

2.4.2 In view of this finding, an evaluation of the clarity of the further independent claims is not necessary.

3. In view of the above finding, an evaluation concerning the further grounds of refusal is not necessary.

4. *Reimbursement of the appeal fee*

According to Rule 103 EPC, the appeal fee shall be reimbursed in the event of interlocutory revision or where the board of appeal deems an appeal to be allowable, if such reimbursement is equitable by reason of a substantial procedural violation. As neither of these alternatives occurs in the present case, the appeal fee cannot be reimbursed.

**Order**

**For these reasons it is decided that:**

1. The appeal is dismissed.
2. The appeal fee is not reimbursed.

The Registrar:

The Chairman

N. Maslin

U. Oswald