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# D E C I S I O N
# of 2 May 2005

**Case Number:** T 0062/00 - 3.3.2

**Application Number:** 89302746.6

**Publication Number:** 0333523

**IPC:** A61K 9/50

**Language of the proceedings:** EN

**Title of invention:**
Method of potentiating an immune response and compositions therefor

**Patentee:**
THE UAB RESEARCH FOUNDATION, ET AL

**Opponent:**
Chiron Corporation
Alkermes, Inc.

**Headword:**
-

**Relevant legal provisions:**
EPC Art. 123(2), 123(3)

**Keyword:**
"Allowability of amendments (no)"
"Main request and first auxiliary request (Article 123(3) EPC): Scope of amended claims exceeds scope of claims as granted"
"Second and third auxiliary request (Article 123(2) EPC): Generalisation not possible"

**Decisions cited:**
G 0001/03, G 0002/03

**Catchword:**
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Beschwerdekammern | Boards of Appeal | Chambres de recours

**Case Number:** T 0062/00 - 3.3.2

# D E C I S I O N
**of the Technical Board of Appeal 3.3.2**
**of 2 May 2005**

**Appellant:** (Proprietor of the patent)
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**Decision under appeal:**
**Decision of the Opposition Division of the European Patent Office posted 23 December 1999 revoking European patent No. 0333523 pursuant to Article 102(1) EPC.**

**Composition of the Board:**

**Chairman:** U. Oswald
**Members:** H. Kellner
P. Mühlens

## Summary of Facts and Submissions

I. European patent No. 0 333 523 based on application No. 89 302 746.6 was granted with 30 claims for contracting states DE, GB, FR, IT, NL, SE, CH, LI, BE, AT and LU and 23 claims for contracting states ES and GR.

Independent claims 1, 18, 24 and 28 as granted for the contracting states other than ES and GR read as follows:

"1. A composition for delivery of bioactive agent to the mucosally associated lymphoreticular tissue of a human or other animal comprising:

biocompatible microcapsules comprising a bioactive agent encapsulated in a biocompatible excipient and having a size of from 1 µm to less than 5 µm, for selective absorption by and passage through mucosally associated lymphoreticular tissue for providing systemic immunity, and

biocompatible microcapsules comprising the bioactive agent encapsulated in a biocompatible excipient and having a size of between 5 µm and 10 µm, for selective absorption and retention by mucosally associated lymphoreticular tissue for providing mucosal immunity,

as a combined preparation for potentiating the immune response of a human or other animal.

18. A composition for potentiating the immune response of a human or other animal comprising microcapsules having a size between 1 µm and 10 µm containing

bioactive agent encapsulated in a biocompatible excipient, wherein the composition is adapted exclusively for parenteral administration, provided that the excipient is not a proteinoid or polyacryl starch.

24. A composition for potentiating the immune response of a human or other animal, comprising a mixture of a first free bioactive agent to provide a primary response and biocompatible microcapsules having a size of between 1 μm and 10 μm and containing a second bioactive agent encapsulated in a biocompatible excipient for release pulsatily to provide a subsequent response.

28. A method of preparing a pharmaceutical composition, comprising encapsulating a bioactive agent selected from antigens, allergens, lymphokines, cytokines, monokines and immunomodulator agents in a biocompatible excipient to form microcapsules having a size of between 1 μm and 10 μm and formulating a bioactive agent selected as aforesaid in free form and the microcapsules into the composition."

II. Opposition was filed against the granted patent under Article 100(a) and (c) EPC.

III. By its decision pronounced on 18 November 1999 and posted on 23 December 1999, the opposition division revoked the patent under Article 102(1) EPC because neither the set of claims of the main request nor the sets of claims of the first and third auxiliary requests filed in writing and during the oral proceedings met the requirements of Article 123 EPC.

The second auxiliary request was not admitted into the proceedings as it had been filed late and related to "prima facie" problems regarding Rule 57a EPC and Article 123(2) EPC.

The opposition division noted that the sets of claims of the main request and of the first auxiliary request contained disclaimers that did not fulfil the requirements of Article 123(2) EPC.

The third auxiliary request disclosed the feature "an injectable composition" which was regarded as extending the scope of the claims as granted, thus violating Article 123(3) EPC.

IV. The appellant (patentee) lodged an appeal against said decision and submitted 16 sets of claims as main request and seven auxiliary requests.

It stated that there had been a substantial procedural violation, as it had not had sufficient opportunity to submit auxiliary requests in response to discussion of the formal issues during the oral proceedings before the opposition division. The appellant accordingly wanted the appeal fee to be reimbursed and the case, based on one of its requests, remitted for examination of the issues of novelty and inventive step by the opposition division in a different composition.

V. Dated 4 January 2005, a communication was sent out, drawing the parties' attention to the decisions of the Enlarged Board of Appeal with respect to disclaimers G 1/03, OJ EPO 2004, 413, and G 2/03, OJ EPO 2004, 448,

and to possible problems concerning Articles 84 and 123(2) and (3) EPC and Rules 57(1), 57a and 58(2) EPC.

The appellant was particularly requested to indicate where the basis for all amendments in the current claims could be found both in the application as filed and in the specification of the patent as granted. Particular attention was drawn to the fact that any new wording, included in claims as granted or in further amended claims, must appear in the same context as the wording in the application as filed.

In the event that the new wording in amended claims differed from the wording in the application as filed, the appellant was requested to submit thorough explanations showing why the new wording did not change the originally disclosed subject-matter.

VI. With a letter dated 3 March 2005, the appellant introduced six sets of claims for the two different groups of contracting states as the new main request and first and second auxiliary requests.

The subject-matter of claim 1 of the main request for the contracting states other than ES and GR is based on claims 18 and 19 as granted; it reads as follows:

"Use of microcapsules comprising an antigen encapsulated in a biocompatible excipient wherein the excipient comprises a poly(DL-lactide-coglycolide), a poly(L-lactide), a poly(DL-lactide), a poly(glycolide), a copolyoxalate, a polycaprolactone, a poly(lactide-co-caprolactone), a poly(esteramide), a polyorthoester, a poly (ß-hydroxybutyric acid) or a polyanhydride or a

mixture thereof and having a size between 1 µm and 10 µm for preparing an injection for increasing the level of an antibody response in a human or other animal."

The only substantial difference in the corresponding claim 1 of the first auxiliary request with respect to claim 1 of the main request is the change of the words "an injection" after "... for preparing" into the words "a vaccine composition to be administered by injection".

The subject-matter of claim 1 of the second auxiliary request for the contracting states other than ES and GR is based on claim 24 as granted; the wording of claim 1 of the second auxiliary request is as follows:

"A composition for potentiating the immune response of a human or other animal, comprising a mixture of a first free bioactive agent to provide a primary response and biocompatible microcapsules having a size of between 1 µm and 10 µm and containing a second bioactive agent encapsulated in a biocompatible excipient for release pulsatily to provide a subsequent response."

VII. On 2 May 2005 oral proceedings took place before the board in the presence of representatives of the appellant and representatives of opponent 02; duly summoned, opponent 01 had informed the board in advance that it did not wish to attend the hearing.

VIII. During the oral proceedings the appellant introduced a third auxiliary request. The wording of the single claim of this request for the contracting states other than ES and GR is as follows:

"Use of microcapsules comprising an antigen encapsulated in poly(DL-lactide-coglycolide) and having a size between 1 µm and 10 µm for preparing an injection for increasing the level of an antibody response in an animal."

IX. The appellant mainly argued that all claims on file had been reworded in order to overcome the objections raised and were deemed to be allowable with regard to formalities as on the merits.

The subject-matter of claim 1 of the main request was restricted to the use of one of the excipients from the list contained in this claim in order to overcome problems with the disclaimer in the patent as granted.

The different wording in claim 1 of the main request and claim 1 of the first auxiliary request with respect to the use of the composition "for preparing an injection" or "to be administered by injection" was used to overcome problems discussed before the opposition division.

As far as the wording "Use for ... increasing the level of an antibody response" was concerned, the appellant referred to chapter III A in the granted patent and in the application as filed, particularly to example 2 of chapter III A 2, this chapter being entitled "Mechanism of the Adjuvant Effect Imparted by Microencapsulation".

With respect to the claims of the second auxiliary request, it pointed out that they did not differ from claims 24 to 30 as granted. They were originally

disclosed in claims 15 to 19 and claim 47 in the application as filed. Additionally, the definition of "microcapsules" and "encapsulating" in the first pages of the description was important for their understanding. The wording "provide a subsequent response" should have the same meaning as "potentiate a subsequent response" because of the common word "subsequent".

The subject-matter of the claim of the third auxiliary request was restricted to features disclosed in examples 1 and 2 of chapter III A 2 as cited above, in connection with the headline of chapter III A "Vaccine-Microcapsules Administered by Injection". These examples, in the context of the general information given under chapter III A in the application as filed, disclosed all the features contained in this claim.

X. The respondents' arguments submitted in writing and during the oral proceedings may be summarised as follows:

In their view, the opposition division's opinion was right with respect to the formal assessment of the case and with respect to its decision concerning Rule 57 EPC and Article 123 EPC. In the event of remittal to the first-instance department, they requested consideration of the issues of insufficiency, novelty and inventive step without any alteration in the composition of the opposition division.

With respect to the requests on file, it was pointed out that they were regarded as late-filed and not admissible because they were not occasioned by

particular topics arising in the course of the current discussion.

Moreover, claim 1 of the main request and the first auxiliary request violated Article 123(3) EPC because of the wording "wherein the excipient comprises ....", giving a wider scope than granted claim 18, which contained the wording "provided that the excipient is not a proteinoid or polyacryl starch". While not making any comments on the second auxiliary request, the respondent (opponent 02) stated that the subject-matter of the third auxiliary request was also wider in scope than the corresponding claim as granted (Article 123(3) EPC) and that it contained unallowable generalisations with respect to the particular features of examples 1 and 2 of chapter III A 2 as originally filed (Article 123(2) EPC).

XI. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of one of the main, first or second auxiliary requests filed with the letter dated 3 March 2005 or on the basis of the third auxiliary request filed in the oral proceedings.

The respondent (opponent 02) requested that the appeal be dismissed; the respondent (opponent 01) had requested in writing that the appeal be dismissed.

## Reasons for the decision

1. The appeal is admissible.

2. All requests represent a response to the arguments set out in the communication of the board and during the oral proceedings. They have to be regarded as an attempt to overcome the problems discussed by narrowing the scope of the subject-matter of the patent in suit and they were therefore admitted into the proceedings.

3. *Main request and first auxiliary request*

Since the wording "wherein **the excipient comprises** a poly(DL-lactide-coglycolide), a poly(L-lactide), a poly(DL-lactide), a poly(glycolide), a copolyoxalate, a polycaprolactone, a poly(lactide-co-caprolactone), a poly(esteramide), a polyorthoester, a poly (ß-hydroxybutyric acid) or a polyanhydride or a mixture thereof", contained in claim 1 of these requests (bold letters by the board), allows any other substance to be present as an excipient in addition to the substances mentioned in the list, even a proteinoid or a polyacryl starch may be part of the excipient mixture.

Proteinoid and polyacryl starch, however, are disclaimed in the corresponding claim 18 as granted.

Consequently, the range of possible excipients is wider in amended claim 1 of these requests than it was in the patent as granted. This is a violation of Article 123(3) EPC.

4. *Second auxiliary request*

The subject-matter of claim 1 of the second auxiliary request is directed to a composition comprising, inter alia, "biocompatible microcapsules having a size of between 1 µm and 10 µm and containing a second bioactive agent encapsulated in a biocompatible excipient". In the description of the patent in suit as filed in the original application, the term "encapsulation" is defined. It means that the agent to be encapsulated can be coated with a single wall of polymeric material (microcapsules), or can be homogeneously dispersed within a polymeric matrix (microspheres) (see application as filed, page 1, line 25, to page 1a, line 2).

Thus, claim 1 of the second auxiliary request is directed both to microcapsules containing the agent coated in a wall and to microspheres containing the agent homogeneously dispersed within a polymeric matrix.

Claim 15 as originally filed and representing the original disclosure with respect to this claim 1 in suit, however, discloses only "microcapsules having a biocompatible excipient wall and containing a second bioactive agent" and no "microspheres containing homogeneously dispersed agent".

Accordingly, the subject-matter of claim 1 of the second auxiliary request extends beyond the contents of the application as filed and does not meet the requirements of Article 123(2) EPC.

5. *Third auxiliary request*

5.1 There is only one part in the disclosure as filed, wherein the claimed features

- poly(DL-lactide-coglycolide)
- size between 1 µm and 10 µm
- for increasing the level of an antibody response in an animal

are set out in aggregation.

This is example 2 of chapter III A 2, this chapter being entitled "Mechanism of the Adjuvant Effect Imparted by Microencapsulation" (see page 29 of the description as filed for the headline and page 31 for the example).

The headline to example 2 is

"Retarding the Antigen Release Rate
- from 1-10 Micrometer Microcapsules
- Increases the Level of the Antibody Response
and Delays the Time of the Peak Response".

"Enterotoxoid" is used as the antigen contained within a wall matrix of DL-PLG in four different batches of microcapsules. The ability of the different batches of microcapsules to induce a plasma antitoxin response following IP-injection was measured (see page 31, lines 8 to 27, of the description as originally filed; DL-PLG is defined as poly(DL-lactide-coglycolide) on page 19, line 29, together with the corresponding header of this example 2 on page 15; for the definition

of "IP-injection" see page 27, line 13, and "enterotoxoid" is "Staphylococcal Enterotoxin B Vaccine" from the definitions on page 23, lines 6 to 24, particularly line 21).

The remaining features in the claimed "use of microcapsules comprising

- an antigen
- encapsulated ...
- for preparing an injection ...",

however, are generic terms not contained in example 2 as such, and a generalisation of the specific teaching of said example 2 is not allowable.

The reasons are that

- enterotoxoid cannot be used as a model substance for any possible antigen, increasing the level of an antibody response in an animal,
- microcapsules containing the agent within a wall matrix cannot be used as a model system for microspheres containing the agent homogeneously dispersed in the excipient, and
- an IP-injection cannot be used as model application for any type of injection, albeit intravenous, subcutaneous or intramuscular alternatively.

Consequently, the claim of the third auxiliary request contravenes Article 123(2) EPC.

5.2 In these circumstances, the arguments of the respondent cannot succeed:

The respondent submitted that there were parts of the text under section "A. Vaccine-Microcapsules Administered by Injection.", including the headline itself, that gave general advice with respect to the subject-matter of the patent in suit and not only information restricted to the local paragraphs. Additionally, the definition of the term "encapsulated" in the application as filed, page 1, line 25, to page 1a, line 2, showed that the applicants did not really want to make a difference between microcapsules containing the agent in a wall of excipient, and microspheres having the agent homogeneously dispersed in the excipient.

However, even if parts of the disclosure have already been used to find necessary general definitions such as "IP-injection" and "enterotoxoid", at least during the oral proceedings the appellant was unable to indicate any particular parts rectifying the generalisations contained in the third auxiliary request.

Particularly the headline of section A., containing the general term "injection", also stands for the use of microcapsules

- "less than 10 microns, preferably less than 5 micrometers, or more preferable 1 to 5 micrometers" (see page 34 of the description as filed, lines 18 to 20)

or microcapsules

- "greater than 5 micrometers, preferably greater than 10 microns, but not so large that they cannot be

administered for instance by injection, preferably less than 250 micrometers" (see page 34, lines 27 to 30)

and is not typical of microcapsules of a size between 1 µm and 10 µm. The generic feature "use of microcapsules for preparing an injection" under discussion and exclusively concerning microcapsules "sized between 1 µm and 10 µm" cannot thus be derived from this headline.

With respect to the term "encapsulated" contained in the third auxiliary request, it is pointed out that its definition, given in the first pages of the description as filed, means precisely that there is a difference between the agent contained in a wall of excipient and the agent which is homogeneously dispersed. Only for the purposes of the description in the patent in suit should the terms "microcapsules" and "encapsulated" stand for both variants.

Thus, the agent contained in a wall, as set out in example 2 of chapter III A 2, can only refer to one of the variants, while the term "encapsulated" in the third auxiliary request by definition means both.

Consequently, the second possibility is not disclosed in the context of said example 2 and, precisely because of the definition of "encapsulated", a generalisation is not possible.

6. Accordingly, claim 1 of the main request as well as claim 1 of the first, second and third auxiliary requests contravene Article 123 EPC.

**Order**

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

The appeal is dismissed.

The Registrar: The Chairman:

A. Townend U. Oswald