

BESCHWERDEKAMMERN
DES EUROPÄISCHEN
PATENTAMTS

BOARDS OF APPEAL OF
THE EUROPEAN PATENT
OFFICE

CHAMBRES DE RECOURS
DE L'OFFICE EUROPEEN
DES BREVETS

Internal distribution code:

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

**Datasheet for the decision
of 19 February 2009**

Case Number: T 1139/06 - 3.3.02

Application Number: 93922577.7

Publication Number: 0663840

IPC: A61K 49/00

Language of the proceedings: EN

Title of invention:
Preparation of microcapsules

Patentee:
Quadrant Drug Delivery Limited

Opponent:
Advanced Inhalation Research Inc
BOEHRINGER INGELHEIM PHARMA GmbH & CO. KG

Headword:
Preparation of Microcapsules/QUADRANT DRUG DELIVERY LTD.

Relevant legal provisions:
EPC Art. 54, 56, 83, 84, 123(2), 123(3), 111

Relevant legal provisions (EPC 1973):

-

Keyword:

"Admissibility - (no): auxiliary request IV late filed"
"Added matter - (yes): combination of 2 ranges not originally disclosed"
"Extension of protection conferred - (no): change of category from product to method of preparation allowable"
"Priority - (yes): Priority document constitutes the first disclosure of the subject-matter of auxiliary request V"
"Clarity, sufficiency - (yes): determination of human circulation $t_{1/2}$ common general knowledge"
"Novelty - (yes): Subject-matter of auxiliary request V not specifically disclosed in prior art"
"Inventive step - (yes): opponent's argumentation solely based on post-published document"

Decisions cited:

G 0002/88

Catchword:

-



Case Number: T 1139/06 - 3.3.02

DECISION
of the Technical Board of Appeal 3.3.02
of 19 February 2009

Respondent: Advanced Inhalation Research Inc
(Opponent I) 88 Sidney Street
Cambridge
Massachusetts 02139 (US)

Representative: Chapman, Paul William
Kilburn & Strode
20 Red Lion Street
London WC1R 4PJ (GB)

Appellant: BOEHRINGER INGELHEIM PHARMA GmbH & CO.KG
(Opponent II) A Patente
D-55216 Ingelheim/Rhein (DE)

Representative: Nühning, Anja
Fuchs, Georg Ludwig
BOEHRINGER INGELHEIM PHARMA GmbH & CO.KG
Patent Department
Binger Str. 173
D-55216 Ingelheim/Rhein (DE)

Appellant: Quadrant Drug Delivery Limited
(Patent Proprietor) 1 Mere Way
Ruddington
Nottingham, NG11 6JS (GB)

Representative: Bassett, Richard Simon
Potter Clarkson LLP
Park View House
58 The Ropewalk
Nottingham, NG1 5DD (GB)

Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
30 May 2006 concerning maintenance of European
patent No. 0663840 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: A. Lindner
C. Vallet

Summary of Facts and Submissions

- I. European patent No. 0 663 840 based on application No. 93 922 577.7 was granted on the basis of a set of 25 claims.

The independent claims read as follows:

"1. Hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μm range and at least 90% have a diameter within the range 10.1 to 19.9 μm .

2. Hollow microcapsules in which the interquartile range of diameters is 2 μm or less and the median diameter is between 10.1 μm and 19.9 μm inclusive.

3. Hollow microcapsules with proteinaceous walls in which at least 90% of the microcapsules have a diameter in the range 1.0-8.0 μm ; at least 90% of the microcapsules have a wall thickness of 40-500 nm; at least 50% of the protein in the walls of the microcapsules is so cross-linked as to be resistant to extraction in 1 % HCl for 2 mins; and the microcapsules either have an *in vivo* $t_{1/2}$ of at least 5 minutes or are adapted for selective targeting to an area of the human or animal body.

5. Hollow microcapsules predominantly of 1.0-10.0 μm in diameter, at least 10% of the microcapsules when suspended in water, being capable of surviving a 0.25 s application of a pressure of 2.66×10^4 Pa without bursting, collapsing or filling with water, wherein the microcapsules either have an *in vivo* $t_{1/2}$ of at least

5 minutes or are adapted for selective targeting to an area of the human or animal body.

6. Hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μm range and at least 90% have a diameter within the range 1.0-8.0 μm , and the microcapsules either have an *in vivo* $t_{1/2}$ of at least 5 minutes or are adapted for selective targeting to an area of the human or animal body.

7. Hollow microcapsules in which the interquartile range of diameters is 2 μm or less, the median diameter is between 2.0 μm and 8.0 μm inclusive and the microcapsules either have an *in vivo* $t_{1/2}$ of at least 5 minutes or are adapted for selective targeting to an area of the human or animal body.

8. A method of generating an image for subsequent inspection, comprising (a) injecting into the body of a mammal microcapsules according to any one of Claims 1 to 7, (b) subjecting the mammal or part thereof to suitable ultrasonic radiation and (c) detecting ultrasonic radiation reflected, transmitted, resonated or frequency modulated by the said microcapsules.

9. A pharmaceutical composition suitable for intra-arterial administration, comprising hollow microcapsules predominantly of diameter 10.1 to 19.9 μm .

10. A method of generating an image for subsequent inspection, comprising (a) injecting into the body of a mammal microcapsules predominantly of diameter 10.1-19.9 μm , (b) subjecting the mammal or part thereof to

suitable ultrasonic radiation and (c) detecting ultrasonic radiation reflected, transmitted, resonated or frequency modulated by the said microcapsules.

11. A process comprising the step of atomising a solution or dispersion of a wall-forming material in a liquid carrier into a gas in order to obtain hollow microcapsules by evaporation of the liquid carrier, wherein the microcapsules are of 10.1-19.9 μm diameter, or have a human circulation $t_{1/2}$ of at least 5 minutes, or are adapted for selective targeting to an area of the human or animal body.

18. Microcapsules obtainable by a process according to any one of Claims 11 to 17.

19. The use of hollow microcapsules, of which at least 90% have a diameter of between 10.1 and 19.9 μm , in the preparation of a pharmaceutical composition for intra-arterial administration to a human or animal such that the microcapsules deposit in the vasculature.

23. A process of forming microcapsules comprising the step of atomising a solution or dispersion of a wall-forming material in a liquid carrier into a gas in order to obtain hollow microcapsules by evaporation of the liquid carrier, wherein the microcapsule walls have in or on them a polycationic substance, such as polylysine.

25. Hollow microcapsules according to any one of Claims 3 to 7, wherein hyaluronic acid is included in or on the walls of the microcapsules."

II. Two notices of opposition were filed. The patent was opposed under Article 100(a) EPC for lack of novelty and inventive step and under Article 100(b) EPC for insufficient disclosure.

III. The following document was *inter alia* cited during the opposition and appeal proceedings:

(1) WO 92/18164

IV. In the decision pronounced on 4 April 2006, the opposition division found that, account being taken of the amendments made by the patentee during the opposition proceedings, the patent and the invention to which it related in the form of auxiliary request III met the requirements of the EPC. Its principal findings were as follows:

In connection with the main request in the form of the claims as granted, the opposition division came to the conclusion that the subject-matter of claim 11 was not novel over document (1).

As regards auxiliary requests I and II, the opposition division found that the requirements of Article 123(2) and (3) EPC were not met. In addition, it was concluded that the subject-matter of auxiliary request II was not in accordance with the requirements of Article 84 EPC either. With reference to Rule 71(a) EPC, the opposition division decided not to admit auxiliary requests I and II into the proceedings.

Regarding auxiliary request III, it was found that the requirements of Articles 84, 123(2) and (3), 54 and 56

EPC as well as of Rule 71(a) EPC were met. In connection with the requirements of Article 56 EPC, the opposition division acknowledged an inventive step over document (1), which had been identified as closest prior art, on account of an improved echogenicity combined with the absence of adverse hemodynamic effects, which were obtainable with the claimed microcapsules.

- V. The patentee and opponent II lodged an appeal against that decision.
- VI. With the statement of the grounds of appeal, the appellant-patentee filed auxiliary requests I to VII.
- VII. With his letter dated 19 January 2009, the appellant-patentee filed an amended auxiliary request III.
- VIII. In a fax dated 12 February 2009, the board issued its preliminary opinion in connection with sufficiency, clarity and inventive step.
- IX. With a fax dated 17 February 2009, the appellant-patentee filed auxiliary requests Ia, IIIa, IVa, VII and VIII.
- X. At the oral proceedings on 19 February 2009, the appellant-patentee filed a new main request and 5 auxiliary requests.
- XI. The wording of the relevant independent claims is as follows:
 - (a) Main request:

"1. Hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μm range and at least 90% have a diameter within the range 12 to 19.9 μm ."

(b) Auxiliary request I:

"1. Use of a block copolymer of the poloxamer series to coat microcapsules in order to provide them with a human circulation $t_{1/2}$ of at least 5 minutes, the microcapsules being:

- Hollow microcapsules predominantly of 1.0-10.0 μm in diameter, at least 10% of the microcapsules when suspended in water, being capable of surviving a 0.25 s application of a pressure of 2.66×10^4 Pa without bursting, collapsing or filling with water, or
- Hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μm range and at least 90% have a diameter within the range 1.0-8.0 μm , or
- Hollow microcapsules in which the interquartile range of diameters is 2 μm or less, the median diameter is between 2.0 μm and 8.0 μm inclusive.

2. Use of a material that changes the charge of microcapsules to selectively target the microcapsules to an area of the human or animal body, the microcapsules being:

- Hollow microcapsules predominantly of 1.0-10.0 μm in diameter, at least 10% of the microcapsules when suspended in water, being capable of surviving a 0.25 s application of a pressure of 2.66×10^4 Pa without bursting, collapsing or filling with water, or
- Hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μm range and at least 90% have a diameter within the range 1.0-8.0 μm , or
- Hollow microcapsules in which the interquartile range of diameters is 2 μm or less, the median diameter is between 2.0 μm and 8.0 μm inclusive,

the said material being included in or on the wall of the microcapsules.

5. The use of hollow microcapsules, of which at least 90% have a diameter of between 10.1 and 19.9 μm , in the preparation of a pharmaceutical composition for intra-arterial administration to a human or animal such that the microcapsules deposit in the vasculature."

(c) Auxiliary request II:

Independent claims 1 and 2 of auxiliary request II are identical to claims 1 and 2 of auxiliary request I.

(d) Auxiliary request III:

Claim 1 of auxiliary request III is identical to claim 1 of auxiliary request I.

"2. Use of a material that is a positively or negatively charged polyamino acid, a phospholipid, hyaluronic acid or polygluconic acid to change the charge of microcapsules to selectively target the microcapsules to an area of the human or animal body, the microcapsules being:

- Hollow microcapsules predominantly of 1.0-10.0 μ min diameter, at least 10% of the microcapsules when suspended in water, being capable of surviving a 0.25 s application of a pressure of 2.66×10^4 Pa without bursting, collapsing or filling with water, or
- Hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μ m range and at least 90% have a diameter within the range 1.0-8.0 μ m, or
- Hollow microcapsules in which the interquartile range of diameters is 2 μ m or less, the median diameter is between 2.0 μ m and 8.0 μ m inclusive,

the said material being included in or on the wall of the microcapsules."

(e) Auxiliary request IV:

Claim 1 of auxiliary request IV is identical to claim 1 of auxiliary request I.

"2. Use of a material that is a phospholipid or hyaluronic acid to change the charge of microcapsules

to selectively target the microcapsules to an area of the human or animal body, the microcapsules being:

- Hollow microcapsules predominantly of 1.0-10.0 μm in diameter, at least 10% of the microcapsules when suspended in water, being capable of surviving a 0.25 s application of a pressure of 2.66×10^4 Pa without bursting, collapsing or filling with water, or
- Hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μm range and at least 90% have a diameter within the range 1.0-8.0 μm , or
- Hollow microcapsules in which the interquartile range of diameters is 2 μm or less, the median diameter is between 2.0 μm and 8.0 μm inclusive,

the said material being included in or on the wall of the microcapsules, and the microcapsules being a dry powder."

(f) Auxiliary request V:

The sole independent claim 1 of auxiliary request V is identical to claim 1 of auxiliary request I.

XII. The appellant-patentee's arguments can be summarised as follows:

(a) Admissibility:

As regards the admissibility of the new requests, and in particular of the main request and auxiliary requests I, II and III, it was argued that no new features were introduced as compared to the previous requests on file. Moreover, the various deletions, which simplified the further procedure, were to be seen as a reaction to the board's communication of 12 February 2009. The filing of auxiliary requests IV and V was the consequence of objections raised at the oral proceedings.

(b) Main request:

In connection with the amendments made in claim 1 of the main request, it was held that, as the original application disclosed a range of 10.1 to 19.9 μm and a further range of 12 to 25 μm , which both related to the same type of microcapsules, it was allowable to take the lower endpoint of one range and the upper endpoint of the other range for defining a new range from 12 to 19.9 μm .

(c) Auxiliary request I:

As regards the alleged extension of the protection conferred, it was emphasised that the subject-matter of claims 1 and 2 of auxiliary request I concerned a process for preparing microcapsules as defined in the claims as granted. Such a change of claim category was allowable under Article 123(3) EPC.

In connection with the clarity of the feature human circulation $t_{1/2}$, it was reasoned that differences caused by injections at different sites of the body were negligible, as the microcapsules, once injected into the bloodstream, circulated very rapidly.

As for the novelty of claims 1 and 2 of auxiliary request I, reference was made to the features "...in order to provide them with a human circulation $t_{1/2}$ of at least 5 minutes" (claim 1) and "...to selectively target the microcapsules to an area of the human or animal body" (claim 2). These effects, which had to be taken into consideration in a use claim, were not disclosed in document (1) in connection with block copolymers of the poloxamer series and with a material that changed the charge of microcapsules, respectively.

(d) Auxiliary request V:

The appellant-patentee contested that document (1) constituted the first disclosure of the invention. As a consequence, the priority was valid for the claims of auxiliary request V.

In connection with inventive step, it was held that document (1) did not constitute a state of the art applicable for the requirements of Article 56 EPC.

XIII. The arguments submitted by appellant-opponent II and the respondent can be summarised as follows:

(a) Admissibility:

In view of the numerous requests already submitted by the appellant-patentee and the very late filing of the new requests, all requests filed at the oral proceedings of the board were considered to be inadmissible.

(b) Main request:

As regards the amendments made in claim 1 of the main request, it was held that the feature "at least 90% have a diameter within the range of 12 to 19.9 μm " was not originally disclosed.

(c) Auxiliary request I:

As for claim 1 of auxiliary request I, it was argued that not all block copolymers of the poloxamer series were able to direct microcapsules away from the microcapsules when injected into the blood circulatory system. As a consequence, the deletion of this feature extended the protection conferred. Moreover the deletion of the feature that the microcapsules were injected was not allowable under Article 123(2) EPC either.

Furthermore, in view of the fact that the original application did not describe any method for determining the human circulation $t_{1/2}$, this feature was not allowable under Articles 83 and 84 EPC. A further objection under Article 84 EPC was raised in connection with the percentages, as it was not clear whether percent by

weight, percent by volume or another calculation base was meant.

In addition, appellant-opponent II held that example 1 of document (1) was detrimental to the novelty of claim 1 of auxiliary request I. The subject-matter of claim 2 was also anticipated by document (1).

(d) Auxiliary request V:

In connection with the validity of the priority of auxiliary request V, it was not contested that the subject-matter as claimed therein was disclosed in the priority document. Appellant-opponent II, however, reasoned that the priority document did not constitute the first disclosure of the invention as required by Article 87 EPC. It was held that document (1), which had also been filed by the patentee, contained the first disclosure of the subject-matter of auxiliary request V. As a consequence, the priority was not valid.

As for the inventive step of auxiliary request V, it was held that the subject-matter claimed therein was obvious in the light of the teaching of document (1).

XIV. The appellant-patentee requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request or of one of the 5 auxiliary requests filed during the oral proceedings.

Furthermore, the appellant-patentee requested the remittal to the first instance.

The appellant-opponent II requested that the decision under appeal be set aside and that the European patent No. 0663840 be revoked.

Reasons for the Decision

1. The appeal is admissible.
2. Admissibility of the new requests:
 - 2.1 Main request and auxiliary requests I, II and III:

These requests were filed only at an advanced stage of the oral proceedings before the board. However, the amendments made do not introduce any new features as compared to auxiliary requests II and III, filed with letter dated 4 October 2006. Furthermore, the various deletions simplify the procedure and can essentially be seen as a reaction to the board's communication of 12 February 2009. As a consequence, the main request as well as auxiliary requests I, II and III are admissible.

- 2.2 Auxiliary request IV:

Auxiliary request IV was filed at a very advanced stage of the oral proceedings before the board, i.e. at 18.00 hrs. In this request, a new element was introduced into claim 1 that had hitherto played no role at all in the proceedings, namely that the microcapsules are a dry powder. Taking into consideration that this request was filed very late, after numerous auxiliary requests had already been

submitted, and that the other parties were taken by surprise by this amendment so that they were not in a position to appropriately react at this late stage, the board decided not to admit auxiliary request IV into the proceedings.

2.3 Auxiliary request V:

In auxiliary request V, the claimed subject-matter was restricted to a single claim, which is identical to claim 1 of auxiliary request I, which had already been found to meet the requirements of Articles 123(2) and (3), 84 and 54 EPC (see paragraph 4 below). As a consequence, although filed at a very advanced stage of the oral proceedings before the board, the board decided to admit auxiliary request V into the proceedings.

3. Main request - Article 123(2) EPC:

In claim 1, the range of the diameter of at least 90% of the hollow microcapsules was changed from 10.1 to 19.9 μm to 12 to 19.9 μm .

For the "large" microcapsules, the following diameter ranges are disclosed in the original application: 10.1 to 19.9 μm (claim 1), 12 to 25 μm (page 10, lines 23-24 and page 11, line 9), 15 to 20 μm (page 2, line 20) and 13 to 18 μm (page 15, line 8). Although there may be cases where it is possible to define a new range Z with a lower endpoint taken from an original range X and an upper endpoint taken from a different original range Y, the board came to the conclusion that such a

rearrangement was not possible in the present case for the following reasons:

Claim 1 relates to hollow microcapsules having a specific particle size distribution which is defined by a combination of interdependent inseparable features, i.e. by the features that more than 30% of the microcapsules have a diameter within a 2 μm range and at least 90% have a diameter within the range 10.1 to 19.9 μm . The fact that a first population A of microcapsules is characterised by more than 90% of the microcapsules having a diameter within the range of 10.1 to 19.9 μm and a second population B of microcapsules by more than 90% of the microcapsules having a diameter within the range of 12 to 25 μm does not automatically imply that more than 90% of a new population C have a diameter within the range of 12 to 19.9 μm . Thus, the population A mentioned above includes compositions in which a high proportion of microcapsules is within the range of 10.1 to less than 12 μm and a proportion of close to 10% has a diameter of above 19.9 μm . Cutting off the range from 10.1 to < 12 μm results in a population of microcapsules in which less than 90% of the microcapsules are within the claimed range of 12 to 19.9 μm .

Likewise, the second population B mentioned above includes compositions in which a high proportion of microcapsules is within the range of > 19.9 μm to 25 μm and a proportion of close to 10% has a diameter of < 10.1 μm . Again, by discarding the range from > 19.9 μm to 25 μm , a new population of microcapsules is obtained, wherein less than 90% of the microcapsules are within the claimed range of 12 to 19.9 μm .

It follows therefrom that, in order to arrive at the population of hollow microcapsules as claimed in claim 1 of the main request, selections have to be made from the entirety of the original populations A and B, for which there is no basis in the original application.

The appellant-patentee additionally referred to the disclosure on page 15, lines 6-8 of the original application, where at least 90% of the microcapsules have a diameter within the range of 13 to 18 μm , and argued that in such a composition the concentration of microcapsules having a diameter in the range of 12 to 19.9 μm must also be at least 90%. However, by extending the range from originally 13 to 18 μm to 12 to 19.9 μm , the concentration of 90% is also shifted to a higher value of e.g. 92 or 93% in consequence of this extension. In other words, a composition in which at least 90% of the microcapsules have a diameter within the range of 13 to 18 μm does not specifically disclose a composition, in which the percentage of microcapsules having a diameter within the range of 12 to 19.9 μm is exactly 90%.

Further selections which have no basis in the original application must be made when a further limitation of claim 1 is taken into consideration, namely that more than 30% of the microcapsules have a diameter within a 2 μm range. As there are no further indications about the exact position of this 2 μm range within the wider range of 10.1 to 19.9 μm , the population A mentioned above includes compositions in which the more than 30% of the microcapsules having a diameter within a 2 μm

range are predominately in the range of 10.1 to < 12 μm . Likewise, population B comprises compositions in which the more than 30% of the microcapsules having a diameter within a 2 μm range are in the range of > 19.9 to 25 μm .

In both cases, the new population C would be characterised by less than 30% of the microcapsules having a diameter within a 2 μm range.

For all these reasons, the subject-matter of claim 1 of the main request does not meet the requirements of Article 123(2) EPC.

4. Auxiliary request I:

4.1 Amendments - Article 123(2) EPC:

4.1.1 Claim 1:

The use of the block copolymers of the poloxamer series as claimed in claim 1 is based on the passages on page 20, lines 17-21 and the paragraph bridging pages 20 and 21 of the original application. In this context, it is noted that the passage on page 20, lines 17-18 does not specifically relate to the human circulation time, but to the circulation time in the body in general. However, the fact that the coated or "long life" microcapsules have a prolonged human circulation time is derivable from the disclosure of the original application in its entirety (see e.g. page 2, lines 18-23).

The three distinct types of microcapsules which are defined in the latter part of claim 1 correspond to the microcapsules of original claims 3, 5 and 7, except for the replacement of the terms "hollow microsphere" and "in vivo $t_{1/2}$ " (original claims) by "hollow microcapsule" and "human circulation $t_{1/2}$ " (present claim 1). As for the former amendment, it is noted that the terms "hollow microsphere" and "hollow microcapsule" were used synonymously and interchangeably in the original application. As a consequence, this replacement does not change the subject-matter as claimed at all. As for the second replacement, reference is again made to page 20, lines 17-21 and the paragraph bridging pages 20 and 21 of the original application, where the (human) circulation $t_{1/2}$ is disclosed for the coated long life microcapsules.

In the light of this disclosure in the original application, the board cannot follow the argumentation of the respondent, according to which claim 1 must comprise the feature that the microcapsules are injected into the blood circulatory system in order to be allowable under Article 123(2) EPC. As a consequence, the subject-matter of claim 1 meets the requirements of Article 123(2) EPC.

4.1.2 Claim 2:

The inclusion of a material that changes the charge of microcapsules to selectively target the microcapsules to an area of the human or animal body in or on the wall of the microcapsules is disclosed on page 17, line 30 to page 18, line 6 of the original application. As regards the original disclosure of the three

distinct types of microcapsules, see paragraph 4.1.1 above, which applies *mutatis mutandis* to the subject-matter of claim 2. As a consequence, the requirements of Article 123(2) EPC are met.

4.2 Clarity:

4.2.1 Claim 1:

4.2.1.1. Human circulation time:

Parameters such as the human circulation $t_{1/2}$ are allowable under Article 84 EPC only if they can be clearly and reliably determined either by indications in the description or by objective procedures which are usual in the art.

In the present case, the description does not contain any indications as to how the human circulation $t_{1/2}$ was determined. While it does not appear necessary to describe how to measure the human circulation $t_{1/2}$, as the person skilled in the art would know how to draw a blood sample and subsequently determine the concentration of microcapsules in that sample, the board had concerns that the human circulation $t_{1/2}$ might be highly dependent on the exact site where the microcapsules are introduced into the body. Thus, microcapsules injected close to the heart might have a human circulation $t_{1/2}$ which is quite different from that of the same microcapsules when introduced e.g. into the lower limbs.

However, the appellant-patentee argued that substances circulate very quickly in the bloodstream, so that

differences in the human circulation $t_{1/2}$ caused by different sites of application are negligible compared to the time span of at least 5 minutes as claimed. In the absence of any counter-arguments from appellant-opponent II and the respondent, the board sees no reason to contest this reasoning. As a consequence, the parameter "human circulation $t_{1/2}$ " is allowable under Article 84 EPC.

4.2.1.2. Definition of the term "percent":

As was correctly pointed out by appellant-opponent II, there is no information in the original application as to whether the percentages used in claim 1 relate to percent by weight, percent by volume or to any other calculation base. The absence of such information does not, however, result in any ambiguity; it simply means that the claimed percentages must be fulfilled for any calculation base.

As a consequence, the subject-matter of claim 1 meets the requirements of Article 84 EPC.

4.2.2 Claims 2 and 6:

The reasoning of paragraph 4.2.1.2 above applies *mutatis mutandis* to the subject-matter of claims 2 and 6. As a consequence, the requirements of Article 84 EPC are met.

4.3 Sufficiency of disclosure:

In the light of the finding in paragraph 4.2.1.1 above, the absence of a method for determining the human

circulation $t_{1/2}$, which had been objected to by appellant-opponent II under Article 83 EPC, does not lead to any problems concerning sufficiency of disclosure either. As a consequence, the requirements of Article 83 EPC are also met.

4.4 Extension of the protection conferred - Article 123(3) EPC:

4.4.1 Claim 1:

Before a conclusion can be drawn as to whether the subject-matter of claim 1 is allowable under Article 123(3) EPC, it has first to be decided which category of use this claim pertains to: whether it exclusively relates to the use of a compound for obtaining a certain effect, i.e. to the use of a block copolymer of the poloxamer series for providing microcapsules with a human circulation $t_{1/2}$ of at least 5 minutes, or whether it concerns a process for preparing the microcapsules. In the former case, claim 1 would not be allowable under Article 123(3) EPC, as the totality of the subject-matter of the claims as granted does not encompass the use of a block copolymer of the poloxamer series for obtaining such an effect.

However, the wording of claim 1 reads "Use of a block copolymer of the poloxamer series **to coat** microcapsules in order to provide them with a human circulation $t_{1/2}$ of at least 5 minutes...". As coating constitutes an activity associated with the preparation of microcapsules, the board came to the conclusion that the subject-matter of claim 1 is directed to a method of preparing microcapsules, as was asserted by the

appellant-patentee. The various microcapsules prepared by the method according to present claim 1 are included in claims 5, 6 and 7 as granted except for the replacement of "in vivo $t_{1/2}$ " by "human circulation $t_{1/2}$ " (see paragraph 4.1.1 above). As already pointed out by the opposition division (see paragraph B.1 of the contested decision), the "in vivo $t_{1/2}$ " encompasses e.g. "tissue $t_{1/2}$ " and is therefore broader than the term "human circulation $t_{1/2}$ ". It follows therefrom that the subject-matter of present claim 1 concerns a method for preparing microcapsules which are encompassed by the microcapsules as defined in claims 5, 6 and 7 as granted. As a product claim covers all methods for making the same, the board sees no problem under Article 123(3) EPC with regard to the change of claim category from a product to a process for its preparation.

4.4.2 Claim 2:

Again, it has to be established in a first step whether the subject-matter of present claim 2 is exclusively directed to the use of a compound for obtaining a certain effect, i.e. to the use of a material that changes the charge of microcapsules for selectively targeting the microcapsules to an area of the human or animal body, or whether it concerns a process for preparing microcapsules. Again, the board came to the conclusion that the claimed subject-matter defines a process for preparing hollow microcapsules which are encompassed by the microcapsules as defined in claims 5, 6 and 7 as granted. As a consequence, the reasoning of paragraph 4.4.1 above applies *mutatis mutandis* to

the subject-matter of claim 2, which therefore also meets the requirements of Article 123(3) EPC.

4.4.3 Claim 6:

Claim 6 corresponds to claim 19 as granted. The requirements of Article 123(3) EPC are therefore met.

4.5 Novelty:

4.5.1 Claim 1:

Reference is made to paragraph 4.4.1 where it was reasoned that the subject-matter of claim 1 is directed to a process for preparing microcapsules.

Example 1 of document (1) describes a method for preparing hollow microcapsules by atomising a 20% solution of rHA. The intermediate microcapsules thus obtained then undergo heat fixation. In a further step, they are milled in a mixture with lactose. This mixture is then resuspended in water containing 1 mg/ml Pluronic F68 (block copolymer of the poloxamer series). It follows therefrom that example 1 of document (1) describes the use of a block copolymer of the poloxamer series to coat microcapsules. However, neither example 1 nor the subsequent examples based on example 1 specifically disclose microcapsules comprising all the features of the three types of microcapsules defined in present claim 1.

4.5.1.1. As regards the first type of microcapsules of present claim 1, there is no specific disclosure in document (1) that the microcapsules of example 1 or of the

subsequent examples are capable of surviving a 0.25 s application of a pressure of 2.66×10^4 Pa without bursting, collapsing or filling with water. Hollow microcapsules predominantly of 1.0-10 μm in diameter comprising this resistance to outside pressure are disclosed on page 15, lines 9-14 and in claim 17 of document (1), but not in context with block copolymers of the poloxamer series. Therefore, document (1) is not detrimental to the novelty of claim 1 as far as the preparation of the first type of microcapsules is concerned.

4.5.1.2. In connection with the second and third types of microcapsules of present claim 1 it is noted that the examples of document (1) do not specifically disclose the preparation of hollow microcapsules in which more than 30% of the microcapsules have a diameter within a 2 μm range (second type) or in which the interquartile range of diameters is 2 μm or less (third type).

As a consequence, the subject-matter of claim 1 of auxiliary request I is novel over document (1).

4.5.2 Claim 2:

Document (1) discloses a process for preparing hollow microcapsules by atomising a solution of a microcapsule-forming agent, preferably a proteinaceous material such as human serum albumin, and then insolubilising the microcapsules (see page 2, lines 6-9, 15-16; page 6, lines 9-16). The preparation to be sprayed may contain additional substances which are listed on page 7, line 25 to page 8, line 27. This list of compounds includes substances such as polyglutamic

acid (page 8, line 3), which, being ionic, changes the charge of microcapsules. This general disclosure of preparing hollow microcapsules is applicable to all types of microcapsules subsequently described, including the microcapsules defined on page 15, lines 9-14 (which correspond to the first type of microcapsules of present claim 2), the microcapsules defined in the paragraph bridging pages 13 and 14 (which correspond to the second type of microcapsules of present claim 2) and the microcapsules defined on page 14, lines 3-4 (which correspond to the third type of microcapsules of present claim 2). It follows therefrom that document (1) discloses the inclusion of a material that changes the charge of microcapsules into or onto the wall of microcapsules as defined in present claim 2. It therefore has to be evaluated whether or not the feature "use of a material that changes the charge of microcapsules **to selectively target the microcapsules to an area of the human or animal body**", which constitutes the only potentially distinguishing feature of the claim, can establish novelty.

As was pointed out in paragraph 4.4.2 above, the subject-matter of claim 2 concerns a process for preparing hollow microcapsules. A process for preparing a composition is defined by the various process steps which are necessary in order to obtain the desired composition. The above feature, however, defines an effect of a compound used in the preparation of microcapsules, which has no influence whatsoever in their preparation: in both document (1) and the patent under appeal, the charged compound is preferably added to the wall-forming material before spray-drying (see

page 7, lines 25-27 of document (1) and page 18, lines 25-29 of the original application). As a consequence, the above feature has merely an explanatory function and cannot therefore render novel the process for preparing hollow microcapsules as claimed in claim 2 of auxiliary request I. In this context, it is noted that, in view of the fact that the subject-matter of claim 2 concerns a process for preparation rather than a use of a compound for obtaining an effect, decision G 002/88 (OJ 1990, 093) does not apply in the present case. The requirements of Article 54 EPC are therefore not met.

4.5.3 In the light of the above finding, an evaluation of the novelty of independent claim 6 is not necessary.

5. Auxiliary request II:

Claim 2 of auxiliary request II is identical to claim 2 of auxiliary request I. As a consequence, the requirements of Article 54 EPC are not met for the same reasons as outlined in paragraph 4.5.2 above.

6. Auxiliary request III:

Claim 2 of auxiliary request III is identical to claim 2 of auxiliary request I, except that the material that changes the charge of microcapsules is now limited to a negatively charged polyamino acid, a phospholipid, hyaluronic acid and polygluconic acid. In view of the fact that in document (1) the list of compounds that may be added to the wall-forming material includes substances such as polyglutamic acid (negatively charged polyamino acid), the reasoning of paragraph 4.5.2 applies *mutatis mutandis* to claim 2 of

auxiliary request III. As a consequence, the requirements of Article 54 EPC are not met.

7. Auxiliary request V:

7.1 Novelty:

Claim 1 of auxiliary request V is identical to claim 1 of auxiliary request I. As a consequence, the subject-matter as claimed therein is novel over document (1) for the same reasons as outlined in paragraph 4.5.1 above.

As none of the other documents cited in the course of the proceedings relates to the use of block copolymers of the poloxamer series for preparing hollow microcapsules, the subject-matter of claim 1 of auxiliary request V meets the requirements of Article 54 EPC.

7.2 Validity of the priority:

As the fact that the subject-matter of auxiliary request V is disclosed in the priority document was not contested by appellant-opponent II and the respondent, the only question to decide is whether the priority document constitutes the first application of the invention as required by Article 87 EPC or whether the appellant-patentee had already disclosed this invention in document (1). In this context, reference is made to paragraph 4.5.1, where the board came to the conclusion that the subject-matter of claim 1 was novel over document (1). It follows therefrom that the priority document constitutes the first application in the sense

of Article 87 EPC. As a consequence, the priority is valid for the subject-matter as claimed in auxiliary request V.

7.3 Inventive step:

In view of the fact that the priority date of 10 October 1992 is the effective filing date for the subject-matter of auxiliary request V, document (1), which was published on 29 October 1992, does not constitute prior art applicable for inventive step.

Although the appellant-opponent II and the respondent were repeatedly informed by the board that post-published document (1) did not constitute state of the art for inventive step, they nevertheless based their reasoning exclusively on document (1) and did not cite any other evidence. Therefore, the board concluded that the argumentation with regard to lack of inventive step was not well founded. As a consequence, the board, being satisfied that the subject-matter of auxiliary request V is not obvious in the light of the common knowledge of the person skilled in the art, decides that the requirements of Article 56 EPC are met.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to grant a patent on the basis of auxiliary request V and a description to be adapted.

The Registrar:

The Chairman:

N. Maslin

U. Oswald