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**Datasheet for the decision
of 26 June 2009**

Case Number: T 0535/07 - 3.3.02

Application Number: 95110723.4

Publication Number: 0681843

IPC: A61K 49/22

Language of the proceedings: EN

Title of invention:

Preparation of diagnostic agents

Patentee:

Quadrant Drug Delivery Limited

Opponent:

Advanced Inhalation Research Inc.

Headword:

Diagnostic Agents/QUADRANT DRUG DELIVERY LTD.

Relevant legal provisions:

EPC Art. 123(2)

Relevant legal provisions (EPC 1973):

-

Keyword:

"Main request, auxiliary requests 1-5: admissibility - (yes);
added matter (yes) - combination of features not originally
disclosed"

"Auxiliary request 6: admissibility (no): late filed and prima
facie not allowable"

"Auxiliary request 7: not open to discussion in view of
G 0009/92"

Decisions cited:

G 0009/92

Catchword:

-



Case Number: T 0535/07 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 26 June 2009

Appellant: Quadrant Drug Delivery Limited
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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
2 February 2007 concerning maintenance of the
European patent No. 0681843 in amended form.

Composition of the Board:

Chairman: M. C. Ortega Plaza
Members: A. Lindner
J.-P. Seitz

Summary of Facts and Submissions

- I. European patent No. 0 681 843 based on application No. 95 110 723.4, which is a divisional application of application No. 92 303 236.1, was granted on the basis of a set of 9 claims.

The independent claims read as follows:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution or dispersion of a wall-forming protein or polysaccharide material in a liquid carrier into a gas, to obtain the hollow microcapsules by evaporation of the liquid carrier, substantially without reducing the water-solubility of at least the outside of the microcapsules.

6. Microcapsules obtainable by a process according to any of claims 1 to 5, of which more than 30% have a diameter within a 2 μm range and at least 90% have a diameter of 1 to 8 μm ."

- II. An opposition was filed against the granted patent. The patent was opposed under Article 100(a) EPC for lack of novelty and lack of inventive step, under Article 100(b) EPC for insufficient disclosure of the invention and under Article 100(c) EPC for amendments that contain subject-matter extending beyond the content of the application as originally filed.

III. The present appeal lies from an interlocutory decision of the opposition division to maintain the patent in amended form based on the auxiliary request 2, filed during the oral proceedings before the opposition division.

The independent claims of auxiliary request 2 read as follows:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution of a wall-forming protein material in an aqueous liquid carrier into a gas, to obtain the hollow microcapsules by evaporation of the liquid carrier, wherein the microcapsules comprise 96-98% monomeric protein and the process does not comprise a second step of reducing the water-solubility of at least the outside of the microcapsules.

5. Microcapsules obtainable by a process according to any of claims 1 to 4, of which more than 30% have a diameter within a 2 μm range and at least 90% have a diameter of 1 to 8 μm ."

IV. The opposition division found that both the main request and auxiliary request 1 contained subject-matter that extended beyond the content of the application as filed. As regards auxiliary request 2, the opposition division concluded that the subject-matter claimed therein met the requirements of Articles 123(2), 123(3), 83, 54 and 56 EPC.

- V. The appellant (patentee) lodged an appeal against that decision. In the statement of the grounds of appeal, the appellant argued that the main request as well as auxiliary request 1 met the requirements of Article 123(2) EPC. Moreover, auxiliary requests 3 to 10 were filed.
- VI. In its letter dated 5 December 2007, the respondent (opponent) contested the argumentation of the appellant.
- VII. With letter dated 20 March 2008, the appellant additionally filed auxiliary requests 11 and 12.
- VIII. In its letter dated 18 June 2008, the respondent raised objections under Articles 123(3) and 54 EPC in connection with auxiliary request 11.
- IX. In the annex to the summons to oral proceedings sent on 25 March 2009, the board expressed its preliminary opinion with regard to the requests on file. The board noted that the subject-matter of the main request as well as claim 1 of auxiliary request 1 did not appear to meet the requirements of Article 123(2) EPC. Moreover, the board made reference to decision G 0009/92, OJ EPO 1994, 875, and informed the parties that auxiliary request 2 was not open to discussion.
- X. With letter dated 26 May 2009, the appellant filed auxiliary requests 1 to 16.
- XI. Oral proceedings took place on 26 June 2009. At the oral proceedings, the appellant filed auxiliary requests 1 to 7.

Moreover, the appellant withdrew auxiliary requests 8 to 16.

The independent process claims of auxiliary requests 1 to 6 read as follows:

(a) Auxiliary request 1:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution of a wall-forming protein material in a liquid carrier into a gas, to obtain the hollow microcapsules by evaporation of the liquid carrier, substantially without reducing the water-solubility of at least the outside of the microcapsules".

(b) Auxiliary request 2:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution of a wall-forming protein material in an aqueous liquid carrier into a gas, to obtain the hollow microcapsules by evaporation of the liquid carrier, substantially without reducing the water-solubility of at least the outside of the microcapsules".

(c) Auxiliary request 3:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution of a wall-forming protein material in a liquid carrier into a gas, to obtain the hollow microcapsules by evaporation of the liquid carrier, substantially without reducing the water-solubility of at least the outside of the

microcapsules, wherein the microcapsules are non-toxic and non-immunogenic".

(d) Auxiliary request 4:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution of a wall-forming protein material in a liquid carrier into a gas in a chamber, to obtain the hollow microcapsules by evaporation of the liquid carrier, substantially without reducing the water-solubility of at least the outside of the microcapsules, wherein the outlet temperature of the gas is 40 to 150°C".

(e) Auxiliary request 5:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution of a wall-forming protein material in a liquid carrier into a gas, to obtain the hollow microcapsules by evaporation of the liquid carrier, substantially without reducing the water-solubility of at least the outside of the microcapsules, wherein the microcapsules are 0.1 to 20.0 µm in diameter".

(f) Auxiliary request 6:

"1. A process for preparing hollow microcapsules, which comprises atomising a solution of a wall-forming protein material in a liquid carrier into a gas, to obtain the hollow microcapsules by evaporation of the liquid carrier, substantially without reducing the water-solubility of at least the outside of the microcapsules, wherein more than 30% of the

microcapsules have a diameter within a 2 μm range and at least 90% have a diameter of 1 to 8 μm ".

Auxiliary request 7 was identical to auxiliary request 2 filed before the opposition division, which served as basis for the opposition division's decision of maintenance in amended form.

XII. The appellant's arguments may be summarised as follows:

(a) In connection with the admissibility of the new requests the appellant submitted that all amendments were of a simple and straightforward nature, which did not take the respondent by surprise. Moreover, the number of requests was considerably reduced.

(b) As regards the requirements of Article 123(2) EPC, claim 1 of the main request was not to be construed such that a first step was carried out substantially without reducing the water-solubility of at least the outside of the microcapsules. Rather, claim 1 meant that the microcapsules, once formed, did not have their water solubility **subsequently** reduced. This interpretation was in line with the disclosure on page 2 lines 5-9 of the original application.

(c) Alternatively, the appellant submitted that the original application in its entirety provided a clear basis for the first step being effected substantially without reducing the water solubility of at least the outside of the microcapsules. Thus, it was mentioned on page 3, lines 23-25 that the preparation of the microcapsules could be carried out either as a "single process" or, alternatively, as a two step process.

According to lines 19-20 of the same page, the water-solubility of at least the outside of the microcapsules was reduced in the second step of the process. It followed therefrom that there was no reduction of water-solubility in the first step. Furthermore, the passage on page 12, lines 9-13 revealed that the procedure could be stopped after the first step. As a consequence, there was a clear disclosure in the original application that the preparation of the microcapsules could be restricted to the first step, in which no reduction of the water-solubility occurred.

(d) Further indications could be found on page 11, lines 21-25 and on page 13, lines 4-9, which revealed that **in the "one step version"**, the temperature "may be sufficient to insolubilise at least part of the wall-forming material". From this passage it could be deduced that insolubilisation due to temperature did not occur in the first step of the two step process.

(e) The appellant also referred to figure 2, in which the influence of temperature and length of incubation on the degree of fixation in the second step was shown. The starting point of 100% free monomer, which was the starting point of heating, was the end point of spray-drying. All tests started with 100% of free monomers which showed that no polymerisation and thus no reduction of water-solubility had occurred in the first step. Although figure 2 related to a specific example, in which albumin was used, the disclosure of the examples had a more general character, as albumin was the classic representative of polymers in connection with the microcapsules in question.

(f) Finally, the appellant referred to the passage on page 12, lines 7-9, which mentioned that in the two step process the intermediate microcapsules (i.e. the microcapsules after the first step) "comprised typically 96-98% monomeric HA". In view of the fact that the remaining HA (2-4%) included water-soluble dimers and trimers, this passage constituted a further basis for the water-solubility not being substantially reduced in the first step. The appellant further emphasised that there was no proof for the allegation that there might be an uneven distribution of monomeric HA across the shell of the microcapsules.

(g) As regards the auxiliary requests, the appellant submitted that in view of the amendments made in auxiliary requests 1 and 2 the claimed subject-matter was now closer to the examples. Furthermore, the outlet temperature introduced into claim 1 of auxiliary request 4 defined a temperature range in which no insolubilisation took place. No additional arguments were submitted with regard to the amendments made in auxiliary requests 3 and 5.

XIII. The respondent's arguments may be summarised as follows:

None of the newly filed auxiliary requests 1 to 6 addressed the problems in connection with the requirements of Article 123(2) EPC. As a consequence, these requests were not admissible.

The claims had to be read in their ordinary meaning. Hence, the appellant's attempt to re-construct claim 1 was to be rejected.

As regards the requirements of Article 123(2) EPC, there was no unambiguous disclosure in the original application that the preparation of hollow microcapsules as claimed in claim 1 of all requests on file was carried out without substantially reducing the water-solubility of at least the outside of the microcapsules.

XIV. The appellant requested that the decision under appeal be set aside and that the patent be maintained as granted (Main Request) or subsidiarily on the basis of one of auxiliary requests 1 to 7 filed during the oral proceedings held before the Board of Appeal.

The respondent requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.
2. *Admissibility of the auxiliary requests*
 - 2.1 Auxiliary requests 1 to 6 were filed at a late stage of the appeal proceedings, i.e. at the beginning of the oral proceedings before the board. The admissibility of these requests is therefore at the board's discretion and depends upon the overall circumstances of the case under consideration (see Article 13 RPBA).

2.2 Auxiliary requests 1 to 5:

Apart from minor amendments, auxiliary requests 1, 2, 3, 4 and 5 are identical to the previous auxiliary requests 1, 5, 7, 10 and 12, respectively. The amendments were made either to remove inconsistencies within the claims (auxiliary request 1), to overcome problems regarding the requirements of Article 123(3) EPC (auxiliary request 2) or to further delimit the subject-matter of the claims from the prior art (auxiliary requests 3 to 5). Moreover, the amendments were of a simple nature which could not take the respondent by surprise. The board therefore decided to admit auxiliary requests 1 to 5 to the proceedings (Article 13 RPBA).

2.3 Auxiliary request 6:

Claim 1 of auxiliary request 6 corresponds to claim 1 of previous auxiliary request 11 except that the features "dispersion" and "polysaccharide" were deleted which means that the atomisation step is now mandatorily carried out with a solution of a wall-forming protein material in a liquid carrier. As the board had *prima facie* serious doubts that the original application contained a specific disclosure of the combination of all the features of claim 1 and as the appellant, having already filed numerous requests before, submitted this request at a very late stage of the appeal procedure, the board decided not to admit auxiliary request 6 into the appeal proceedings (Article 13 RPBA).

2.4 Auxiliary request 7, filed at the oral proceedings before the board, is identical to auxiliary request 2 which was filed during the oral proceedings before the opposition division and which served as basis for the maintenance of the patent in amended form.

Since the opponent did not file an appeal against the interlocutory decision of the opposition division, auxiliary request 7 (previous auxiliary request 2) is a secured fall back position for the appellant in the present appeal procedure (see G 009/92, principle of prohibition of *reformatio in peius*). Thus, the admissibility of auxiliary request 7 cannot be questioned.

3. *Added matter (Article 100(c) EPC)*

3.1 *Main request*

3.1.1 As far as the process claim 1 is concerned, the board is convinced that, on a natural reading, the feature "substantially without reducing the water-solubility of at least the outside of the microcapsules" concerns the entire process claimed rather than only a period subsequent to the formation of the intermediate microcapsules as alleged by the appellant (see point XII, paragraph (b) above). Thus, the process claimed in claim 1 requires that during the formation of the microcapsules no substantial reduction of the water-solubility of at least the outside of the microcapsules must occur.

3.1.2 As regards the disclosure in the application as filed of the feature "substantially without reducing the water-solubility of at least the outside of the microcapsules" in claim 1 of the main request, the following has to be said:

The process claimed in claim 1 corresponds to the first step in the preparation of hollow microcapsules as defined on page 3, lines 14-17 of the original application, which may or may not be followed by a second step, in which the water-solubility of at least the outside of the microcapsules is reduced (see page 3, lines 19-21 of the original application).

Having regard to the claim's wording, the crucial point is to assess whether or not the original application discloses directly and unambiguously that the first step is carried out substantially without reducing the water-solubility of at least the outside of the microcapsules.

The original application does not contain an explicit disclosure of this feature, as all the passages depicting the feature "substantially without reducing the water-solubility of at least the outside of the microcapsules" specifically relate to the second step (see page 3, lines 19-21; page 12, lines 15-19 and claim 2 of the original application).

Additionally, as already mentioned above, the original application discloses *inter alia* a two step process for preparing hollow microcapsules, in which the first step comprises the preparation of the microcapsules. In the subsequent second step, the water-solubility of at

least the outside of the microcapsules is reduced (see page 3, lines 19-21 and 23-25). Furthermore, the second step is optional, as the procedure can be stopped after the first step (see page 12, lines 9-13).

However, the fact that an optional second step is disclosed, in which the water-solubility of at least the outside of the microcapsules is reduced, does not provide an unambiguous basis for the first step being carried without substantially reducing the water-solubility of at least the outside of the microcapsules. It is not excluded that said water-solubility is already "substantially reduced" in the first step and then **further** reduced in the optional second step.

Neither does the disclosure on page 11, lines 21-25 and page 13, lines 4-9 provide an unambiguous basis for the contested feature. The mentioned passage indicates that in the one step version (i.e. "single process"), the temperature may be sufficient to insolubilise at least part of the wall-forming material. From the other passages cited above, it cannot be deduced either that insolubilisation effected by temperature **only** occurs in the "single process". In fact, no conclusions can be drawn from the passages quoted above with regard to the temperatures applied in the first step of the two step process.

It follows therefrom that the feature "substantially without reducing the water-solubility of at least the outside of the microcapsules" is not specifically disclosed in the original application in connection with the process of claim 1, either explicitly or implicitly, i.e. said feature is not directly and

unambiguously derivable from the application as filed for the process claimed.

3.1.3 The appellant also referred to figure 2. Figure 2 is based on a specific example (rHA). The features disclosed therein are very much dependent on the specific protein used as well as on the conditions used in said example and cannot therefore be extrapolated to protein material or even polysaccharide material as claimed in claim 1 of the main request. The board does not contest that rHA might constitute the most classic example of a protein typically used in the preparation of hollow microcapsules, as was alleged by the appellant, however other proteins with different properties are included in claim 1. As a consequence, figure 2 and its corresponding example cannot serve as a basis for the contested features in claim 1, since they represent an unallowable generalisation of some specific examples.

Likewise, the passage on page 12, lines 6-12, which indicates that in the two-step process the intermediate microcapsules comprise typically 96-98% monomeric HA cannot serve as a basis for the amendments made in claim 1, as the range of 96-98% concerns a specific wall-forming material processed under specific conditions, which cannot be generalised to the generic subject-matter defined in claim 1 without extending beyond the content of the application as originally filed.

Additionally, the fact that all tests for the second step of the two-step procedure started with 100% of free monomers does not necessarily imply that no

chemical transformation and thus no reduction of water-solubility has occurred in the preceding first step. Reference is made to page 31, lines 11-15 of the original application, which indicates that the percentage of free monomeric rHA was calculated by measuring the monomer concentration of the unfixed microcapsules and representing this figure as a percentage of the monomer concentration of the unfixed microcapsules. This means that the total amount of free monomers, which is not identical to the total amount of rHA in case that polymerisation had taken place during the first step, was defined as 100%. As a consequence, no conclusions as to the degree of polymerisation or the absence of polymerisation in the first step can be drawn from the 100% in figure 2.

3.1.4 Consequently, the main request fails because it includes subject-matter which extends beyond the content of the application as originally filed (Article 100(c) EPC).

3.2 *Auxiliary request 1*

The process claimed in claim 1 of auxiliary request 1 differs from the process according to claim 1 of the main request in that the atomising step is limited to a solution of a wall-forming protein material. The reasons given for the main request apply *mutatis mutandis* to auxiliary request 1, In particular, the generalisation from rHa or HA to protein material is not allowable within the meaning of Article 123(2) EPC for the reasons given above for the main request (see point 3.1.3 above, first two paragraphs). Thus,

auxiliary request 1 fails since the requirements of Article 123(2) EPC are not met.

3.3 *Auxiliary request 2*

The process claimed in claim 1 of auxiliary request 2 differs from the process according to claim 1 of auxiliary request 1 in that the solution for atomisation of the wall-forming protein material is in an **aqueous** liquid carrier. However, this restriction to an aqueous carrier does not challenge to the validity of the arguments displayed above for the main request and auxiliary request 1, which, as a consequence, apply *mutatis mutandis* to claim 1 of auxiliary request 2.

Consequently, auxiliary request 2 fails also, since the requirements of Article 123(2) EPC are not met.

3.4 *Auxiliary request 3*

Claim 1 of auxiliary request 3 differs from claim 1 of auxiliary request 1 in that the microcapsules prepared by the process are defined as "non-toxic and non-immunogenic". Although the passage on page 4, lines 1-4 of the original application indicates that the process conditions may have an influence on whether or not the resulting microcapsules are sufficiently non-toxic and non-immunogenic, there is no teaching in the original application that avoidance of a reduction of the water-solubility of at least the outside of the microcapsules were necessary in order to obtain non-toxic or non-immunogenic microcapsules.

Moreover, the paragraph bridging pages 12 and 13 of the original application clearly shows that this is not the case, i.e. that non-toxic and non-immunogenic microcapsules are obtainable by a process, which includes a substantial reduction of the water-solubility of the microcapsules. As a consequence, the reasons given for the main request above apply *mutatis mutandis* to claim 1 of auxiliary request 3.

Consequently, auxiliary request 3 fails since the requirements of Article 123(2) EPC are not met.

3.5 *Auxiliary request 4*

The process claimed in claim 1 of auxiliary request 4 differs from the process according to claim 1 of auxiliary request 1 by the additional feature that the outlet temperature of the gas is 40 to 150°C.

The appellant argued that by selecting such mild temperatures, unwanted reaction of the protein components leading to a reduction of the water-solubility were avoided. This reasoning cannot succeed for the following reasons: firstly, it is noted that the upper end of this range includes temperatures of up to 150°C, which cannot be considered as being mild, at least not in the context of the process claimed which addresses protein materials. Secondly, the process of claim 1 encompasses all kinds of wall-forming protein materials including protein materials which are sensitive to temperature. As a consequence, the reasons given above for claim 1 of the main request and auxiliary request 1 apply *mutatis mutandis* to claim 1 of auxiliary request 4.

Consequently, auxiliary request 4 fails also, since the requirements of Article 123(2) EPC are not met.

3.6 *Auxiliary request 5*

Claim 1 of auxiliary request 5 differs from claim 1 of auxiliary request 1 by the additional feature that the microcapsules are 0.1 to 20.0 μm in diameter. According to the description, the size range, which characterises the final product (see page 13, lines 11-16 of the original application), can be introduced at any stage of the preparation process, including at the very end (e.g. by removing those microcapsules which are not within the claimed range). As a consequence, there is no functional relationship between the limitation of the size range now defined in claim 1 of auxiliary request 5 and the preparation of the microcapsules including the atomisation and drying steps (spray-drying). Therefore, the reasons given above for the main request and auxiliary request 1 apply *mutatis mutandis* to claim 1 of auxiliary request 4 so that the requirements of Article 123(2) EPC are also not met. Consequently, auxiliary request 5 also fails.

4. *Auxiliary request 7*

As already mentioned in point 2.4 above, auxiliary request 7 corresponds to the former auxiliary request 2, filed during the oral proceedings before the opposition division and which served as basis for the decision of the opposition division to maintain the patent in amended form. As the patentee is the sole appellant in the present appeal procedure, neither the non-appealing

opponent nor the board may challenge the maintenance of the patent as amended in accordance with the interlocutory decision of the opposition division (see decision G 0009/92, OJ EPO 1994, 875).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

N. Maslin

M. C. Ortega Plaza