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D E C I S I O N
of 13 July 2000

Case Number: T 0389/96 - 3.3.2

Application Number: 89308606.6

Publication Number: 0361677

IPC: A61K 47/30

Language of the proceedings: EN

Title of invention:
Polymeric compositions and methods of producing them

Patentee:
Ciba Specialty Chemicals Water Treatments Limited

Opponent:
S.N.F.

Headword:
pH-dependent release/CIBA

Relevant legal provisions:
EPC Art. 123(2),(3), 56

Keyword:
"Inventive step - alternative process - non obviously derivable from the prior art"

Decisions cited:
-

Catchword:

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0389/96 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 13 July 2000

Appellant: (Proprietor of the patent)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 19 April 1996 revoking European patent No. 0 361 677 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: P. A. M. Lançon
Members: C. Germinario
S. C. Perryman

Summary of facts and submissions

I. European patent No. 0 361 677 was granted pursuant to European patent application No. 89 308 606.6 on the basis of a set of 14 claims for all the designated Contracting States.

The text of granted claim 1 reads:

"1. A process of forming a particulate composition comprising particles comprising an active ingredient distributed substantially uniformly through a dried matrix comprising anionic polymeric material wholly or mainly in free acid form, wherein the amount of polymeric material in the particles is at least 0.5 times the weight of active ingredient and is at least 50% of the weight of the matrix, the polymeric material is soluble or swellable in water at a solubilising pH above 7, and the polymeric material at least in the outer surface of the matrix is substantially less soluble or less swellable in water at a pH below the solubilising pH, characterised in that the process comprises forming a dispersion in water immiscible liquid of aqueous particles containing a solution or dispersion of the active ingredient either in an aqueous solution of a salt of the polymer with a volatile amine or in an oil-in-water emulsion of the polymer wholly or mainly in free acid form, and subjecting the dispersion to azeotropic distillation and thereby forming the particles comprising the active ingredient distributed substantially uniformly through a dried matrix comprising the anionic polymeric material wholly or mainly in free acid form."

II. Notice of opposition was filed by the respondent, requesting revocation of the patent under Article 100(a) EPC on the grounds of lack of inventive step, and Article 100(b) and (c).

The following documents were cited, *inter alia*, during the proceedings before the opposition division:

(1) US-A-3 584 113.

III. The opposition division revoked the patent, in the form of both main and auxiliary requests. It held that the main request did not meet the requirements of Article 123(2) EPC since the term "solubilising pH" was not disclosed in the application as filed.

As to the auxiliary request discussed at the oral proceedings, the opposition division expressed the opinion that the particles described in the preamble of the claim were the same as those known from example (4) of document (1), regardless of the admitted difference in the preparation processes. Therefore, an inventive step could only be justified by the step of azeotropic distillation, which was the unique feature imparting novelty to the claimed process. However the use of this technique for recovering and drying polymeric particles produced by emulsion or reverse phase polymerisation was well known from the many documents cited during the proceedings. For this reason, the claimed subject-matter according to the auxiliary request was obviously derivable from the cited prior art.

IV. The appellant lodged an appeal against this decision, and filed on 29 July 1996 a new main request and three auxiliary requests.

At the oral proceedings, which were held on 13 July 2000, the appellant maintained the first auxiliary request of 29 July 1996 as sole request.

V. The text of the valid claim 1 differs from the text of the granted claim 1 in that the expressions "**soluble or swellable**" and "**less soluble or less swellable**" are replaced by "**soluble and swellable**" and "**insoluble and non-swellable**", and in that the word "**polymer**" has been added before "solubilising pH above 7".

The claim now reads:

"A process of forming a particulate composition comprising particles comprising an active ingredient distributed substantially uniformly through a dried matrix comprising anionic polymeric material wholly or mainly in free acid form, wherein the amount of polymeric material in the particles is at least 0.5 times the weight of active ingredient and is at least 50% of the weight of the matrix, the polymeric material is soluble and swellable in water at a polymer solubilising pH above 7, and the polymeric material at least in the outer surface of the matrix is substantially insoluble and non-swellable in water at a pH below the solubilising pH, characterised in that the process comprises forming a dispersion in water immiscible liquid of aqueous particles containing a solution or dispersion of the active ingredient either in an aqueous solution of a salt of the polymer with a volatile amine or in an oil-in-water emulsion of the polymer wholly or mainly in free acid form, and subjecting the dispersion to azeotropic distillation and thereby forming the particles comprising the active ingredient distributed substantially uniformly through

a dried matrix comprising the anionic polymeric material wholly or mainly in free acid form."

VI. The respondent withdrew the opposition on 21 June 2000. Before this step, it had argued in writing that the main and auxiliary requests were not allowable since the expression "soluble and swellable" contravened Article 123(2) and (3) EPC. In fact, the word "or" in the granted claim was exclusive of one of the two possibilities, whereas the word "and", in the amended form, implied the two alternatives as concomitant, essential features.

The same objection under Article 123(2) and (3) EPC applied to the expression "insoluble and non-swellable" in the auxiliary requests.

As to inventive step, the respondent reiterated essentially the same arguments produced by the opposition division in the decision under appeal.

VII. The appellant requested that the decision under appeal be set aside and the patent maintained on the basis of the amended description and claims filed as the first auxiliary request on 29 July 1996 (sole request).

Reasons for the decision

1. The appeal is admissible.

2. The first amendment of the text of the valid claim 1 consists in the addition of the word "*polymer*" before "*solubilising pH above 7*".

The wording of the application as filed, specifically page 3, lines 24 and 25, page 7, lines 25 and 26, and claim 1, makes it plain that the original expression "solubilising pH" refers to the polymeric material forming the matrix of the particles produced. Moreover the new wording results in a more precise definition of the claimed subject-matter, which implies narrowing the protection conferred by the granted claim. Therefore the amendment is in compliance with the requirements of Article 123(2) and (3) EPC.

2.1 A further amendment is the replacement of "*or*" by "*and*" in the text of claims 1 and 6.

The wording with "and" is not only formally disclosed in the text of claim 1 as filed, but it is also substantially consistent with the real behaviour of the particles produced according to example 1, which when passing into an area of higher pH swell to start releasing the active ingredient and eventually or immediately dissolve totally (see last three lines at the bottom of example 1).

As to the breadth of the protection resulting from the amended form, the board holds, bearing in mind the real properties of many polymeric materials, that the use of the word "or" in the granted claim 1 did not identify a situation of exclusive alternatives - that is either soluble or swellable - but a situation in which the two properties are independent one from the other and may or may not co-exist. As a matter of fact well known to the skilled person, a polymer may dissolve or remain insoluble either with or without previous swelling. All the possible situations are equally feasible and covered by the claim as granted. On the contrary, the

replacement of the word "or" by "and" implies the limitation of the scope of the protection to one only of these possibilities.

For these reasons, the amendment does not contravene Article 123(2) and (3) EPC.

2.2 Finally, claim 1 has been amended by replacing the expression "*less soluble and less swellable*" by "*insoluble and non-swellable.*"

The insoluble and non-swellable character of the polymer, below a given pH, is unambiguously disclosed in the application as filed, on page 7, lines 23 and 24. The board also considers that the new expression represents a limitation in scope, of the expression "less soluble and less swellable" provided in the granted claim. For this reason the amendment complies with the requirements of Article 123(2) and (3) EPC.

The description was also modified, to adapt it to the amended claims, by deleting all those passages reflecting subject-matter no longer claimed. The amendments comply with the requirements of Article 123(2) EPC.

2.3 An additional deletion in the description not related to the amendments introduced into the claims but to a comparative reference in example 4 - last three lines of the text - is also allowable under Rule 57a EPC since this amendment was occasioned by a ground of opposition, namely lack of inventive step, invoked by the respondent.

3. Document (1) was considered by the respondent, and the

Opposition Division in its decision, as the closest prior art for the purpose of assessing the present invention.

3.1 The appellant, on the contrary argued that the closest prior art should be prior art relating to enteric compositions.

3.2 Document (1) discloses the preparation of medical formulations in the form of fine polymerised particles having sustained release of the therapeutic activity into different digestive organs. These particles are prepared by spray drying an aqueous solution or suspension containing a therapeutically active ingredient and a water-soluble polymeric resin capable of being converted into the desired powdery polymerized formulation. The release characteristics of the particles thus obtained are expected not to be influenced by the pH values of the liquids in the different digestive organs, since pH dependence is considered by the author of (1) as a drawback of the previously known compositions, as is expressly mentioned in the discussion of the prior art (see column 2, lines 34 to 38). In fact, the formulations of (1) are said to show outstanding sustained release characteristics in both gastric and intestinal fluids (see second paragraph of column 6), as is also illustrated in Figure 3.

3.3 However claim 1 now before the board has been amended to read "....the polymeric material is soluble and swellable in water at a polymer solubilising pH above 7, and the polymeric material at least in the outer surface of the matrix is substantially insoluble and non-swellable in water at pH below the solubilizing

pH.." and so differs from that considered by the Opposition Division in a feature critical in relation to document (1). Whereas the Opposition Division considered that the claimed process could produce inter alia the same product as described in document (1) in example 4 in particular, so that the only question was to decide whether it would be obvious for the skilled person to use azeotropic distillation instead of the spray drying described in document (1), now the wording of claim 1 excludes producing products releasing active ingredients also in gastric fluids, ie at a pH less than 7. Example 4 of document (1) describes a composition in particle form prepared by spray drying a solution containing caffeine as active ingredient and an ammonium salt of polyacrylic acid having a polymerisation degree of 200. The particles of example 4 show always the same solubility characteristics either in a basic or an acid aqueous medium, since, as explained by the appellant, they consist of polyacrylic acid having a low polymerisation degree (ie 200). The board accepts this, as otherwise the product of example 4 would be inconsistent with the aim of document (1) of providing pH-independent release of the active ingredient in both the intestinal and gastric fluids.

3.4 From the foregoing, the process of claim 1 is recognised as novel over document (1). No other more relevant document has been cited by the respondent which could prejudice novelty of the subject-matter of claim 1.

3.5 As document (1) is thus concerned with making a product which cannot be made by carrying out the process now claimed, and is not concerned with a process using

azeotropic distillation, document (1) is not regarded by the board as the closest prior art for the purpose of defining the problem to be solved.

3.6 Rather the closest prior art is represented by the enteric compositions according to the citations, eg WO-A-88/06407, referred to in the introduction of the patent in suit (page 2, second paragraph) where a polymeric coating is applied to the particle the polymer being impermeable at one pH while permeable or soluble at another. These enteric compositions with their coatings thus prevent release of the active ingredient at the acid pH values in the stomach, but allow release in the non-acid pH of the intestine. As stated in the patent in suit the problem with these enteric coatings is that they may not provide an adequate barrier over the total area of every granule or tablet, either because of non-uniformity in the coating or because they are accidentally fractured in the application, thus causing premature release of the active ingredient. Solving this problem could constitute a significant advantage.

3.7 However, there is no evidence before the board of any advantage of the now claimed process over its whole scope over the prior art, so the achievement of such an advantage cannot be included in the formulation of the technical problem. But the achievement of such an advantage is not necessary for the recognition of inventive step, provided what is claimed cannot be derived in an obvious manner from the prior art.

3.8 The problem to be solved is thus to provide an alternative process of preparing enteric compositions.

3.9 The information in the patent is adequate that it is plausible that the problem has been solved, namely that the process can be used to make enteric compositions. In particular the results reported in example 3 show that the release of dye and clay from the compositions of examples 1 and 2, is indeed pH-dependent and increases up to 100% by shifting the pH values from 6.26 to 7.5.

3.10 Even if the skilled person faced with the above problem were to look at document (1), there is nothing here to give a hint that either the spray draying-process here suggested or the polymers here chosen could be modified in a way that would result in an enteric composition. On the contrary, the skilled person would gather that the process here would result in a pH-independent release which could not assist with the problem. That the product made according to document (1) would also have an active ingredient distributed substantially uniformly in a polymer matrix as would the product of the process now claimed, is a similarity to the present invention which could only be seen with the benefit of hindsight.

3.11 Nor do the traditional enteric compositions referred to in the description of the patent is suit give a hint to the skilled person to adopt the process now claimed. There is no suggestion to use the particular form of the polymer set out in the claim together with an azeotropic distillation, nor to choose the ingredients so that carrying out the process results in a particulate composition comprising an active ingredient distributed substantially uniformly throughout the dried matrix. The prior art enteric coatings were of polymer only, and to choose a process which departs

from this would be counter-intuitive.

3.12 Of the other documents on file, which had been introduced by the respondent with the evident intention of showing that azeotropic distillation of emulsions was a technique well known and usual in the polymer production field, the board notes that none of these relate to compositions showing a pH-dependent release of active ingredients or the advantages thereof. As such none of these documents could suggest that azeotropic distillation in the particular form now claimed producing a particulate composition comprising an active ingredient distributed substantially uniformly throughout the dried matrix, would solve the problem posed.

3.14 Inventive step can therefore be recognised from claim 1. As the other claims depend on claim 1, the request as a whole meets the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The matter is remitted to the first instance with the order to maintain the patent on the basis of the amended description and claim filed as first auxiliary request on 29 July 1996.

The Registrar: The Chairman:

M. Dainese P. A. M. Lançon