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D E C I S I O N
of 8 December 1993

Case Number: T 0879/91 - 3.3.3

Application Number: 85304733.0

Publication Number: 0171907

IPC: C08G 63/06

Language of the proceedings: EN

Title of invention:
Copolymer and method for producing the same

Patentee:
Wako Pure Chemical Industries, Ltd., et al

Opponent:
Boehringer Ingelheim GmbH

Headword:
-

Relevant legal norms:
EPC Art. 54, 56

Keyword:
"Novelty (yes, after amendment)"
"Inventive step (yes, after amendment)"

Decisions cited:
G 0002/88, OJ EPO 1990, 93; T 0002/83, OJ EPO 1984, 265

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0879/91 - 3.3.3

D E C I S I O N
of the Technical Board of Appeal 3.3.3
of 8 December 1993

Appellant: (Proprietor of the patent)
Wako Pure Chemical Industries, Ltd.
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Representative:
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Respondent: (Opponent)
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D - 55216 Ingelheim (DE)

Representative:
-

Decision under appeal:
Decision of the Opposition Division of the European Patent Office of 18 April 1991 issued in writing on 12 September 1991 revoking European patent No. 0 171 907 pursuant to Article 102(1) EPC.

Composition of the Board:

Chairman: C. Gérardin
Members: R.A. Lunzer
M.K.S. Aúz Castro

Summary of Facts and Submissions

I. European patent No. 0 171 907 was granted on 11 January 1989 on the basis of application No. 85 304 733.0 filed on 3 July 1985, having a priority date of 6 July 1984 derived from Japanese application No. 140356/84.

II. On 10 October 1989 an opposition was lodged by the Respondent on the grounds of Articles 100(a) and 100(b) EPC, alleging lack of novelty (Article 54 EPC), and lack of inventive step (Article 56 EPC), and lack of sufficiently clear and complete disclosure (Article 83 EPC). The Opponent relied in particular on the following documents:

(1) US-A-4 273 920 and
(2) DE-A-3 345 314.

III. By its decision given orally on 18 April 1991, and issued in writing on 12 September 1991, the Opposition Division revoked the patent. It held, regarding the main request effective for all the designated Contracting States other than Austria, that product Claim 1 as amended lacked novelty over the disclosure of Example A.11 read in the light of Claim 1 of document (2), and that product Claims 2 to 4 lacked novelty over Example A.15 read in the light of Claim 15 of document (2). The subject-matter of those claims also lacked any inventive step over the disclosure of document (1) which the Opposition Division regarded as being the closest prior art. Although Claims 1 to 5 of the auxiliary request for the other Contracting States, and the main request for Austria, were novel, they lacked any inventive step having regard in particular to Example A.11 of document (2), when read in combination with its Claims 1 and 7.

IV. An appeal against that decision was lodged on 7 November 1991, the appeal fee being paid on the same day. Together with the Statement of Grounds of Appeal filed on 21 January 1992, the Appellant submitted five sets of claims to be considered as a main request, and four auxiliary requests.

The counterstatement filed by the Respondent was a short letter dated 20 May 1992, which did not go into the merits of the appeal. Following a brief adverse comment on the patentability of all the other requests, which were directed to a copolymer of lactic acid and glycolic acid, and/or a method for producing such copolymer, the Respondent concluded that by contrast it would raise no objection to the patentability of the five use claims according to the second auxiliary request.

The main claim in accordance with that request reads as follows:

"1. Use of a copolymer to process into an embedded type or microcapsule type of controlled drug release preparation, wherein the copolymer is a copolymer of 50 to 95 weight % of lactic acid and 50 to 5 weight % of glycolic acid, which has a weight-average molecular weight (measured by gel permeation chromatography) of from 5,000 to 30,000 and a dispersity of from 1.5 to 2, and which is free from catalyst residues."

Claims 2 to 5 are dependent claims concerning preferred embodiments of the main claim.

V. In support of the patentability of that subject-matter the Appellant argued that these claims meet all the requirements of patentability. In particular, as far as inventive step is concerned, document (2) contains no suggestion that the copolymer itself has any use other

than as an intermediate for reacting with the amino acid or sterol. The use of the copolymers as defined in Claim 1 of the patent in suit results in a surprisingly enhanced controlled release effect in comparison to (2), as shown by the experimental report submitted.

VI. The Appellant requests that the decision under appeal be set aside, and that the patent be maintained on the basis of the Claims 1 to 5 filed on 21 January 1992 as its second auxiliary request, together with the adapted description which accompanied its letter of 29 November 1993.

VII. The Respondent stated that it did not have any objections to the existing request of the Appellant.

Reasons for the Decision

1. The appeal is admissible.

2. *Admissibility of Amendments*

The Board sees no objection to the amendments to Claim 1 as now formulated. The use of the products in accordance with the alleged invention is disclosed in the application as filed on page 5, line 34 to page 6, line 7, corresponding to page 3, lines 32 to 36 of the patent as granted. As compared with Claim 1 as granted, the amended claim defines the weight-average molecular weight of the lactic acid/glycolic acid copolymer as being "(measured by gel chromatography)", and also adds the feature that it is "free from catalyst residues". Measurement of the weight-average molecular weight by gel chromatography was disclosed in the application as filed page 7, lines 26 to 31 (page 4, lines 36 to 43 of

the patent as granted), while freedom from catalyst residues results automatically from the method used for producing the copolymer which is based on the absence of any catalyst (page 1, lines 1 to 3; page 4, lines 10/11, and page 5, lines 30 to 33 of the application as originally filed, corresponding to page 2, lines 3 and 4; page 2, line 63; and page 3, lines 30 and 31 of the patent as granted).

The introduction of these limitations into the claims reduces their scope. Accordingly, these amendments are admissible for the purposes of Article 123(3) EPC.

The change in the category of the claims, from "product" claims to "use" claims is permissible where, as in the present case, the scope of protection is not extended thereby (G 2/88, OJ EPO 1990, 93). The dependent Claims 2 to 4 correspond to Claims 2 to 4 as granted (in their turn equivalent to Claims 3 to 5 of the application as originally filed) but drafted now in the form of use claims, whilst the present Claim 5 directed to use in conjunction with a steroid hormone, peptide hormone, or anti-tumour agent, although having no direct equivalent in previously formulated claims, falls wholly within the scope of the present Claim 1. These amendments are therefore permissible for the purposes of Article 123(3) EPC.

3. *Novelty*

Document (2), which was relied on as the basis of the finding of lack of novelty in the decision under appeal, relates to a sustained release carrier for pharmaceutically active substances or drugs. Such carriers derived from glycolic and lactic acids have been known for some years, as is confirmed by document (1). The particular proposal of document (2) is to use

for that purpose a lactic acid-glycolic acid oligomer with a molecular weight in the range of 500 to 10 000, the end carboxylic group of which is modified by reaction with an amino acid, or a sterol (Claim 1).

Novelty can thus be acknowledged because the copolymer used in accordance with the patent in suit lacks any amide or ester modifying group. This makes it superfluous to consider the dispersity of the copolymer obtained in Example A.11 of document (2), or further to interpret the specific molecular weight of that copolymer in the light of the range defined in the main claim of that citation.

4. *Closest prior art*

In view of the experimental test report filed together with the Statement of Grounds of Appeal, the Board regards it as more appropriate to start from document (2) for the definition of the technical problem underlying the patent in suit. As stated above, this document describes the use of oligomers of lactic acid and glycolic acid with a molecular weight in the range of 500 to 10 000, and an amide or ester modifying end group, as sustained release carriers for pharmaceutically active substances or drugs (Claims 1 and 8). Such oligomers have the advantage that they do not contain any residual catalyst, since they are prepared in the absence of any catalyst (page 9, line 17 to page 20, line 9). However, the release of active substances and drugs cannot be regarded as optimal. In view of that shortcoming, the technical problem underlying the patent in suit can be defined as the provision of polymers suitable as a base for drug preparations having a better controlled release effect.

According to Claim 1, this problem is solved by using non-modified copolymers of lactic acid and glycolic acid in the weight ratio of 50:50 to 95:5, which have a weight-average molecular weight measured by gel permeation chromatography of from 5000 to 30 000, and a dispersity of 1.5 to 2.0.

In view of the report "Studies of Leuprolide Acetate Release from Microcapsules of Copoly(Lactic/Glycolic) Acid" filed on 21 January 1992, in particular Table 1 which shows that by using such copolymers as carriers a much better slow releasing effect can be obtained, the Board is satisfied that the above-defined technical problem is effectively solved.

5. *Inventiveness*

5.1 The first question which arises is whether it is proper to interpret Example A.11 of document (2), which describes the preparation of an oligomer with a molecular weight of 1900, and containing 84% by weight of units derived from glycolic acid, in the light of the broader range of molecular weight disclosed in Claim 1, i.e. 500 to 10 000. As it appears from the preferred ranges in the description (page 7, line 19 to page 8, line 13), the upper limit of molecular weight should be between 2000 and 3000. In practice, depending on the method used to determine the molecular weight, the latter is about 2100 and 1930 according to Examples A.1 to A.17 (average of the figures given for these oligomers). Furthermore, the discussion of the prior art in the introduction of document (2) (page 5, line 4 to page 6, line 18), in particular the reference to US-A-2 362 511 describing oligomers of lactic acid and glycolic acid with a molecular weight between 1000 and 2000, clearly shows that the products actually

contemplated in document (2) have a comparable molecular weight.

It follows that the teaching of document (2) is clearly limited to proper oligomers, i.e. to copolymers of limited molecular weight.

5.2 The sole fact that document (1) discloses the incorporation of drugs into non-modified copolymers of lactic acid and glycolic acid having a higher molecular weight cannot lead the skilled reader to the solution claimed in the patent in suit.

According to Claim 7 of that citation, copolymers with a molecular weight of between 6000 and 35 000 are prepared in the presence of a strong acid ion-exchange resin. Emphasis is laid on the necessity to eliminate the catalyst residues (column 3, lines 48 to 68; column 4, lines 47 to 51). However, even if it were possible to obtain a product absolutely free from such impurities, which is doubtful in view of the fact that up to 5% of the catalyst may still be present (column 6, lines 8 to 11), this product would not correspond to the copolymer defined in the patent in suit. As demonstrated in Table 1 of the patent in suit, copolymers of lactic acid and glycolic acid have a much higher dispersity when they have been prepared in the presence of a strongly acid ion-exchange resin catalyst than when no catalyst is used, even when their weight-average molecular weights are very similar. In the former case, dispersity increases from 2.43 to 2.80 as the reaction time increases from 12 to 72 hours, whereas in the latter case, in the absence of a catalyst, it remains practically constant at a value of 1.70, irrespective of the increase in reaction time from 12 to 72 hours. For this reason it must be accepted that the non-modified copolymers described in document (1) have a dispersity

of about 2.5, which is well outside the range required by the patent in suit.

5.3 A further point to be considered is the modification of the carboxylic end groups of the oligomers known from document (2). Even when these oligomers contain units derived from hydroxycarboxyilc acids, other than lactic acid and glycolic acid, all the carboxylic groups are modified by reaction with specific aminocarboxylic acids or sterols (page 8, line 17 to page 9, line 16). These modifying groups must thus be regarded as essential features of the products used as carriers, which means that there would be no incentive for the skilled worker to deviate from that teaching in order to achieve a better control of drug release.

5.4 It is not disputed that a combination of features appropriately selected from the disclosures of documents (1) and (2), i.e. high molecular weight without modification of the carboxylic end groups according to document (1), or polycondensation without a catalyst which results in a lower molecular weight, and narrow dispersity according to document (2), could lead to the subject-matter defined in the main claim of the patent in suit. However, in the Board's view, the question is not whether a skilled worker could have selected and combined these features, but whether he would have done so in the expectation of a better control of drug release (cf. T 2/83 "Simethicone Tablet/RIDER, OJ EPO 1984, 265, point 7). For the reasons given above, the Board can only answer this question negatively.

5.5 It follows that the subject-matter now defined in Claim 1 involves an inventive step as required by Article 56 EPC. The dependent Claims 2 to 5 relate to modifications of the use falling wholly within the scope

of Claim 1, and on that ground alone they are entitled to be upheld.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Opposition Division with the order that the patent be maintained on the basis of Claims 1 to 5 referred to in paragraph IV above, with the amended description referred to in paragraph VI.

The Registrar: The Chairman:

E. Görgmaier C. Gérardin