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**Datasheet for the decision
of 30 October 2018**

Case Number: T 0726/16 - 3.3.07

Application Number: 07017089.9

Publication Number: 1870092

IPC: A61K9/16, A61P27/02, A61K31/36

Language of the proceedings: EN

Title of invention:
Ocular implant made by a double extrusion process

Patent Proprietor:
ALLERGAN, INC.

Opponent:
Generics [UK] Limited

Headword:
Double extrusion / ALLERGAN

Relevant legal provisions:
EPC Art. 56, 113(1)

Keyword:
Inventive step - (no)
Appealed decision - sufficiently reasoned (yes)



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Case Number: T 0726/16 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 30 October 2018

Appellant: Generics [UK] Limited
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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 26 January 2016
rejecting the opposition filed against European
patent No. 1870092 pursuant to Article 101(2)
EPC.**

Composition of the Board:

Chairman A. Usuelli
Members: E. Duval
 P. Schmitz

Summary of Facts and Submissions

- I. European patent No. 1 870 092 was granted on the basis of European patent application 07 017 089.9, filed as a divisional application of European patent application 05 814 028.6.

Claim 1 of the patent as granted related to a bioerodible ocular implant comprising an active agent dispersed within a biodegradable, poly(lactic-co-glycolic)acid (PLGA) copolymer matrix, characterised in particular by a 50/50 weight ratio of lactic to glycolic acid monomers in the copolymer and in that the implant was prepared by a method comprising a milling step and double extrusion process.

- II. The patent was opposed on the grounds that its subject-matter lacked novelty and inventive step (Article 100(a) EPC), was not sufficiently disclosed (Article 100(b) EPC) and extended beyond the content of the application as filed (Article 100(c) EPC).

The following document was among those cited during the first-instance proceedings:

D1: WO 02/43785

- III. The appeal of the opponent (the "appellant") lies against the decision of the opposition division to reject the opposition.

In the decision under appeal, the opposition division found that claim 1 of the patent as granted fulfilled the requirements of Articles 76(1) and 123(2) EPC. The opposition division further found the claimed subject-matter to be novel as it differed from the disclosure

of D1 (example 4) by the double extrusion process, which led to a different release profile in the resulting implant. Starting from D1 as the closest prior art, the opposition division considered the claimed subject-matter to be a non-obvious solution to the problem of providing a bioerodible implant with said particular release profile.

- IV. With the statement setting out the grounds of appeal, the appellant requested that the decision under appeal be set aside and that the patent be revoked in its entirety. The appellant also requested reimbursement of the appeal fee because the opposition division had committed a substantial procedural violation in disregarding arguments central to the case.
- V. In its reply to the opponent's appeal, submitted on 11 October 2016, the patent proprietor (the "respondent") requested that the appeal be dismissed and filed auxiliary requests 1 to 4.

The following document D7 was filed with the respondent's reply:

D7: Experimental Test Report

By letter dated 23 July 2018, the respondent filed a new auxiliary request 1 and renumbered the former auxiliary requests as auxiliary requests 2 to 5.

- VI. On 27 September 2018, the Board issued a communication pursuant to Article 15(1) RPBA.

With regard to inventive step, the Board observed that the claimed subject-matter differed from example 4 of D1 by the ratio of lactic to glycolic acid monomers in

the PLGA copolymer. However, the milling and double extrusion product-by-process features did not appear to constitute further differentiating features over D1. As the sole technical effect resulting from the ratio of glycolic to lactic acid was a corresponding rate of degradation, the problem to be solved was seen as the provision of an implant with a desired rate of degradation. Since the claimed ratio of 50/50, as well as its relevance to degradation rate, was known from D1, no inventive step could be acknowledged. This appeared to apply to all the (then) pending requests.

As to the requested reimbursement of the appeal fee, the Board observed that, although not specifically addressing some arguments presented by the opponent, the reasons given in the decision under appeal enabled the parties and the Board to understand why the decision has been taken. Accordingly, the Board was inclined to refuse the request for reimbursement of the appeal fee.

VII. By letter dated 24 October 2018, the respondent filed two new auxiliary requests 2 and 3, and submitted the following document D8:

D8: Declaration of Dr. Salameh

VIII. Oral proceedings took place on 30 October 2018 in the presence of the respondent, but, as had been announced, in the absence of the appellant.

IX. In the oral proceedings, the respondent withdrew the main request and requested that the patent be maintained:

- on the basis of the set of claims filed as auxiliary request 2 by letter of 24 October 2018, which became its main request;
- alternatively on the basis of the set of claims filed as auxiliary request 1 by letter of 23 July 2018;
- or on the basis of the set of claims filed as auxiliary request 3 by letter of 24 October 2018, which became its auxiliary request 2.

X. Claim 1 of the main request read:

"A bioerodible implant for treating an ocular condition comprising an active agent dispersed within a biodegradable polymer matrix, wherein at least 75% of the particles of the active agent have a diameter of less than 10 μm , the biodegradable polymer comprises poly(lactic-co-glycolic) acid (PLGA) copolymer, the ratio of lactic to glycolic acid monomers in the PLGA copolymer is 50/50 weight percentage, and the bioerodible implant is prepared by a method comprising the steps of: (a) milling the PLGA; (b) blending the milled PLGA and the particles of the active agent, to thereby obtain a blended mixture of the milled PLGA and the particles of the active agent; (c) carrying out a first extrusion of the blended mixture, to thereby obtain a first extrusion product; (d) pelletizing the first extrusion product, and; (e) carrying out a second extrusion of the pelletized first extrusion product, thereby obtaining the bioerodible implant".

Claim 1 of auxiliary request 1 differed from claim 1 of the main request by the following additional feature regarding the blended mixture of step (b):

"wherein at least 75% of the particles of the active agent have a diameter of less than 20 μm ".

Claim 1 of auxiliary request 2 differed from claim 1 of the main request by the following additional feature regarding the blended mixture of step (b):

"wherein at least 75% of the particles of the active agent have a diameter of less than 10 μm ".

XI. The appellant requested that the decision under appeal be set aside and that the patent be revoked in its entirety. It also requested reimbursement of the appeal fee.

XII. The appellant's arguments, where relevant for the present decision, may be summarised as follows:

(a) The claimed subject-matter lacked novelty over example 4 of D1. Although not explicitly mentioned therein, the claimed ratio of monomers in PLGA resulted from a selection from a single list in the description ([0041]) of D1. The process features did not establish a difference over D1 since neither the milling step nor the double extrusion step led to any identifiable difference. The only evidence on file (release profiles in figure 15 of the patent in suit) was not a fair comparison with the single extruded implant of D1 and did not reflect the full scope of the claims, which left the process parameters undefined.

(b) Regarding inventive step, D1 was chosen as the closest prior art. Assuming that the claimed implant differed by an unidentified particular release profile resulting from the double extrusion step, the claimed solution could not be seen as

inventive in the light of the teaching of D1 or D2-D3. Alternatively, assuming that the claimed implant differed by the monomer ratio in PLGA, the solution would also be obvious considering that this ratio was particularly preferred in D1.

- (c) The opposition division had committed a substantial procedural violation in disregarding arguments central to the case regarding novelty over D1, namely that:
- (i) the comparison in figure 15 was unfair because the double, but not single, extruded implant was prepared using milled PLGA, and
 - (ii) the double extrusion step was not limiting because other process factors affected implant homogeneity.

The opposition division's statement that the burden of proof still lay with the opponent in this respect was not seen as an adequate response to these arguments. Accordingly, reimbursement of the appeal fee was justified.

XIII. The respondent's arguments, where relevant for the present decision, may be summarised as follows:

- (a) The implant claimed in the main request differed from the disclosure of D1 in respect of three features, namely:
- (i) the ratio of lactic to glycolic acid monomers in PLGA (although a ratio of 50/50 was mentioned in the general description of D1, no information was given as to the ratio used in example 4),

- (ii) the PLGA milling step, which was not mentioned in example 4, and
- (iii) the double extrusion step, which gave rise not only to a different release profile but also to a higher density, as evidenced by experimental report D7. The existence of fundamental differences in the product as a result of the processing technology was further substantiated in declaration D8.

These differences should be acknowledged because the burden of proof remained with the appellant, who had merely submitted arguments but no evidence.

- (b) Starting from D1 as the closest prior art, the effect of the above differences would be both an improved release profile and a higher density, resulting in smaller and less brittle implants. These advantages would not be derivable from the cited prior art.
- (c) The same arguments applied to the subject-matter of auxiliary requests 1 and 2.

Reasons for the Decision

Main request

- 1. Article 100(a) EPC, inventive step
- 1.1 Both parties and the opposition division selected document D1 as the closest prior art. The Board sees no reason to differ.

Document D1 (see example 4 on page 21) discloses the preparation of a posterior eye segment drug delivery system from:

- PLGA with particle sizes of 9-12 μm in diameter, and
- an active substance (dexamethasone) with particle sizes less than approximately 10 μm in diameter.

The components are mixed and subjected to a single extrusion process.

- 1.2 Claim 1 of the main request specifies that the ratio of lactic to glycolic acid monomers in the PLGA is 50/50 weight percentage. D1 does not explicitly indicate the ratio used in example 4. However, the appellant considers this feature to result from a single selection from the list in paragraph [0041]: "The % of polylactic acid in the polylactic acid polyglycolic acid (PLGA) copolymer can be 0-100%, preferably about 15-85%, more preferably about 35-65%. In a particularly preferred embodiment, a 50/50 PLGA copolymer is used".

For the Board, applying the preferred lactic to glycolic acid ratio of paragraph [0041] to example 4 goes beyond the teaching of D1, even taking its whole content into account, and rather amounts to combining separate items belonging to different embodiments. Example 4 of D1 cannot be regarded as a general disclosure within which a particular aspect (the lactic to glycolic acid ratio) can be independently selected. Rather it must be seen as a specific embodiment using a PLGA that necessarily has a specific, yet undisclosed, lactic to glycolic acid ratio, which gives rise to the specific release profiles of tables 5 and 6. There is no reason why the skilled person would necessarily assume example 4 to use a 50/50 lactic to glycolic acid ratio, since D1 generally allows for this ratio to

range from 0 to 100%. There is also no reason to consider the ratio of 50/50 to implicitly result from the remaining information given in example 4.

- 1.3 As to the product-by-process features, they can only contribute to the novelty of the claimed implant insofar as they give rise to a distinct and identifiable characteristic of the product.
 - 1.3.1 The Board concurs with the appellant that the step of milling does not impart any novel characteristics to the claimed implant. In the absence of any limitation as to the conditions of the milling step, and considering that the PLGA particle sizes in D1 (9-12 μm in diameter) do not depart from those reported after milling in the patent in suit (see [0150], no greater than 20 μm), the milling step does not impart any differentiating feature to the implant.
 - 1.3.2 The implant of claim 1 is further defined by a step of double extrusion, specifically by a sequence of (c) first extrusion, (d) pelletizing the first extrusion product and (e) second extrusion. According to the respondent, these steps lead to the following properties: implants prepared by single or double extrusion processes have different release properties, as shown in figure 15 of the patent in suit; a double extruded implant has a higher density and is less brittle than a single extruded one, as shown by test report D7 filed during appeal proceedings.
 - 1.3.3 The Board considers that, while an extrusion step can be expected to affect the properties of the blend or implant, the skilled person would not necessarily assume that repeating this step would decisively further influence said properties (whether release

profile or density). Additionally, as pointed out by the appellant, a number of extrusion parameters (e.g. single/twin screw extruder, temperature, extrusion speed, die geometry and surface) are acknowledged, in the patent in suit (see [0100]), to influence the properties of the resulting implant, including the release profile. Yet none of these parameters are defined in claim 1.

- 1.3.4 The evidence relied on by the respondent regarding the release profile is figure 15 of the patent in suit. As noted above, the preparation process of D1 comprises neither a milling step nor a second extrusion. The comparison of figure 15 between a single extrusion process (as in D1) and a process comprising milling and double extrusion could therefore be regarded as fair, i.e. as potentially showing the effect of the overall product-by-process features of claim 1 on implant properties. However, this evidence is not found convincing for the following reasons:

The release profiles of figure 15 show an essentially identical release at 7 days, a 10-20% higher release at 14 days, and overlapping release values at 21 days. The extent of this effect on the release profile should be assessed in light of the breadth of the claim. Contrary to the respondent's argument, claim 1 allows not only for more or less vigorous extrusion conditions, but also for the use of any type of extruder and therefore extruder length or screw type. Implants produced under such a variety of conditions can be expected to have release profiles differing to a much greater extent than this mere 10-20%. As a result, claim 1 inevitably covers embodiments in which the milling and double extrusion steps are conducted in such mild conditions that the resulting implant release properties do not

differ from those reported in D1 (see example 4, tables 5 and 6).

1.3.5 It is not contested that the appellant, unlike the respondent, did not file experimental data in support of the facts it alleged, but rather argued on the basis of the evidence on file (i.e. figure 15 and the claims). Nonetheless, for the reasons explained above, the Board considers the appellant's case convincing. Consequently, the Board does not agree with the respondent that the burden remains with the appellant to prove that the process does not impart a differentiating feature to the produced implant.

1.3.6 During appeal proceedings, the respondent submitted that the process features of claim 1 gave rise to an additional difference, namely an improved density. The evidence that D7 adduced to this end compares a double extrusion process in given conditions and using a given extruder with a single extrusion using the same extruder under the same or different conditions. However, D7 suffers from the same deficiency as the experiments of the patent, i.e. it does not reflect the full scope of the claim. No conclusion can be drawn from it on the effect of carrying out the double extrusion in much less stringent conditions. In this respect, the question is not whether the teaching of the prior art can be modified (i.e. the single extrusion of D1 carried out more vigorously) so as to obtain the same properties as example 8 of the patent in suit, but rather whether the claim is so broadly defined, in respect of the process conditions, as to cover implants that are undistinguishable from that of D1.

The Board does not doubt that, in the particular conditions used in experimental report D7, an improved density is obtained. Nor does it doubt that, as explained in declaration D8, this may be related to the air entrapped between the pellets or entering the second extruder under the chosen processing conditions. It remains that, in the absence of any limitation as to extruder, extruding conditions and pelletizer, these effects cannot be credibly considered to occur over the whole scope of the claim. According to paragraph [0100] of the patent, "[d]ifferent extrusion methods may yield implants with different characteristics, including but not limited to the homogeneity [...]" (emphasis added by the Board). There is no evidence that variations due to the processing parameters will remain small compared to the alleged large improvement in density due to the double extrusion.

Lastly, contrary to the respondent's opinion and as explained above (see point 1.2), example 4 of D1 is not to be seen as a generic disclosure from which the claimed subject-matter would differ by the double extrusion step while remaining generic in all other aspects. Rather, example 4 of D1 is a specific embodiment characterised by the specific release profiles of tables 5 and 6, even if this example is silent as to the details of the extrusion parameters used. The respondent chose to define the claimed invention (partly) in terms of the process for its preparation, which may lead to difficulties in devising an experiment demonstrating a resulting difference. This, however, cannot exonerate the respondent from its burden to reverse the conclusion above (see point 1.3.5).

- 1.3.7 Accordingly, the claimed implant differs from that of D1 only by the ratio of lactic to glycolic acid monomers.

None of the advantages alleged by the respondent for the claimed implant (release profile, brittleness) are related to this sole differentiating feature. According to the patent in suit (see [0062]), the rate of biodegradation of the polymer is controlled by the ratio of glycolic to lactic acid, the selection of a ratio of 50/50 thus having the technical effect of leading to a corresponding rate of degradation. The problem to be solved may be seen as the provision of an implant with a desired rate of degradation.

- 1.3.8 Considering that the same selected value of 50/50 and the same statement about the relevance of the glycolic acid:lactic acid ratio to the degradation rate appear in D4 (see [0041]), no inventive step can be acknowledged for the claimed subject-matter.

Accordingly, the requirements of Article 56 EPC are not met.

Auxiliary requests 1 and 2

2. Claim 1 of each of auxiliary requests 1 and 2 differs from the main request in that, in the blended mixture of step (b), "at least 75% of the particles of the active agent have a diameter of less than" 20 μm (auxiliary request 1) or 10 μm (auxiliary request 2). These additional features do not establish a further difference over D1 and do not modify the above conclusions regarding inventive step. Accordingly, the requirements of Article 56 EPC are not met by either request.

Request for reimbursement of the appeal fee

3. According to Rule 103(1)(a) EPC, the appeal fee shall be reimbursed if such reimbursement is equitable by reason of a substantial procedural violation.
4. The appellant considers that the opposition division committed such a substantial procedural violation in disregarding arguments central to the case regarding novelty over D1, namely that:
 - (i) the comparison in figure 15 is unfair because the double, but not single, extruded implant was prepared using milled PLGA, and
 - (ii) the double extrusion step is not limiting because other process factors affect implant homogeneity.

The right to be heard under Article 113(1) EPC requires that those involved be given an opportunity not only to present comments (on the facts and considerations pertinent to the decision) but also to have those comments considered, that is, reviewed with respect to their relevance for the decision on the matter (Case Law of the Boards of Appeal, 8th edition 2016., III.B. 2.4.1). However the deciding body is under no obligation to address each and every argument presented by the party concerned, as long as the reasons given enable the parties to understand whether the decision was justified.

Regarding argument (i), the Board concurs with the appellant that the decision does not explain specifically why the additional milling step did not invalidate the comparison of figure 15. As to argument

(ii), the decision does not comment on homogeneity *per se*. Nonetheless, the opposition division briefly addresses the issue of broadness (i.e. the absence of limitation regarding process factors) in claim 1: the decision under appeal (see Reason for the decision, point 12 on novelty) states that "the burden of proof lies with O1 to prove that an implant made by the process disclosed in example 4 of D1 is the same implant as made by the process disclosed in claim 1 of the patent-in-suit". It can also be understood from this statement why, despite argument (i), the opposition division found the claimed subject-matter to be novel. In its view, any deficiency in the patentee's evidence aiming at establishing novelty (in this case figure 15) cannot modify its conclusion if it anyway considers that the opponent should file evidence showing lack of novelty.

In view of the particular circumstances of the case, i.e. the fact that the contentious point was novelty in the context of a product-by-process feature, the opposition division's reasoning, i.e. its conclusion that the opponent had not met its burden of proof, is regarded as an error of judgement rather than a procedural violation. Notwithstanding this conclusion, the Board additionally is of the view that the absence of engagement with the above particular arguments in the decision, even if seen as a procedural violation, could not be regarded as so substantial as to make reimbursement of the appeal fee equitable, since, overall, the reasons for the decision can be understood and the Board was in a position to review the decision and decided in the appellant's favour.

The Board can therefore not accede to the appellant's request for reimbursement of the appeal fee.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.
3. The appellant's request that the appeal fee be refunded is rejected.

The Registrar:

The Chairman:



S. Fabiani

A. Usuelli

Decision electronically authenticated