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Datasheet for the decision of 12 November 2015

Case Number: T 0389/12 - 3.3.07

Application Number: 97931455.6

Publication Number: 1014941

IPC: A61K47/34, A61K9/20

Language of the proceedings: EN

Title of invention:
HOT-MELT EXTRUDABLE PHARMACEUTICAL FORMULATION

Patent Proprietor:
THE BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM

Opponent:
Grünenthal GmbH

Relevant legal provisions:
EPC Art. 54, 111(1)

Keyword:
Novelty of product-by-process claim (yes)
Appeal decision -
remittal to the department of first instance (yes)

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Case Number: T 0389/12 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 12 November 2015

Appellant: (Patent Proprietor)	THE BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM 201 West 7th Street Austin, Texas 78701 (US)
Representative:	Potter Clarkson LLP The Belgrave Centre Talbot Street Nottingham, NG1 5GG (GB)
Respondent: (Opponent)	Grünenthal GmbH Zieglerstrasse 6 52078 Aachen (DE)
Representative:	Bülle, Jan Kutzenberger Wolff & Partner Theodor-Heuss-Ring 23 50668 Köln (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 21 December 2011 revoking European patent No. 1014941 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	J. Riolo
Members:	A. Usuelli
	D. T. Keeling

Summary of Facts and Submissions

I. European patent No. 1 014 941, based on European application No. 97931455.6, was granted on the basis of four claims.

Claim 1 as granted read as follows:

"1. A hot-melt extrudable controlled release pharmaceutical formulation comprising an effective amount of a therapeutic compound, a high molecular weight poly(ethylene oxide), wherein the poly(ethylene oxide) has a molecular weight average of more than 5,000,000 to 10,000,000 Daltons; and a poly(ethylene oxide) having a molecular weight average less than 500,000 Daltons as a plasticizer, wherein the plasticizer amount does not exceed the amount of the high molecular weight poly(ethylene oxide)."

II. The patent was opposed on the grounds of lack of novelty and inventive step (Article 100(a) EPC) and for insufficiency of disclosure (Article 100 (b) EPC). The following document was among those cited during the first-instance proceedings:

D1: EP 661 045

III. By decision posted on 21 December 2011 the opposition division revoked the patent. The decision was based on the granted patent as main request and two sets of claims filed on 3 October 2011 as auxiliary requests 1 and 2.

Claim 1 of auxiliary request 1 differed from claim 1 of the patent as granted in the addition of the following feature at the end of the claim:

"Wherein said formulation is prepared by a process of hot-melt extrusion".

Claim 1 of auxiliary request 2 was identical to claim 1 of the patent as granted.

IV. In its decision the opposition division held that the subject-matter of claim 1 of all the requests was not novel in view of document D1.

In particular, the opposition division observed that Table 4 of document D1 disclosed four compositions comprising acetaminophene as active ingredient, a high molecular weight poly(ethylene oxide) and polyethylene glycol 6000 (PEG6000), i.e. a poly(ethylene oxide) of low molecular weight. These compositions anticipated the subject-matter of claim 1 of the granted patent.

As to the subject-matter of auxiliary request 1, the opposition division expressed the view that the addition of a product-by-process feature, indicating that the formulation was prepared by a process of hot-melt extrusion, did not render novel the claimed subject-matter over the disclosure of D1.

V. The patent proprietor (appellant) lodged an appeal against that decision. With the statement setting out the grounds of appeal filed on 30 April 2012 he maintained the main request (i.e. maintenance of the patent as granted) and submitted five auxiliary requests.

Auxiliary request 1 was identical to auxiliary request 1 forming the basis of the decision under appeal.

With the grounds of appeal the appellant submitted also the following pieces of evidence:

D8: Declaration by Dr Feng Zhang
Exhibit F of D8: International Journal of Pharmaceutics, 269, (2004), 509-522
D9: Declaration by Dr Mark Manning
D10: US2011/0038930

VI. In a communication pursuant to Rule 15(1) RPBA issued on 27 July 2015, the Board expressed the opinion that claim 1 as granted was not novel over D1 while the subject-matter of auxiliary request 1 appeared to comply with the requirement of novelty. In the same communication the Board observed that the possibility of remitting the case to the opposition division for further prosecution should be considered, if one of the requests were considered to comply with the requirements of novelty and sufficiency of disclosure.

VII. The representative of the respondent (opponent) informed the Board by letter dated 12 October 2015 that neither the respondent nor its representative would attend the oral proceedings. In the same letter, the respondent also requested the Board to remit the case to the opposition division if one of the sets of claims were considered to meet the requirements of novelty and sufficiency of disclosure.

VIII. During the oral proceedings held on 12 November 2015 in the absence of the respondent, the appellant withdrew its main request (granted patent). The set of claims

submitted as auxiliary request 1 on 30 April 2012 became the new main request.

IX. The appellant essentially argued that the formulations defined in claim 1 of the main request (previous auxiliary request 1) were to be considered novel over D1 in view of the product-by-process feature recited in the claim. A product of hot-melt extrusion, such as the formulation of claim 1, had very different structural and functional properties from a product of direct compression such as the composition of D1. This was confirmed by the declarations D8 and D9 and by the teaching of D10.

As to the issue of remitting the case to the opposition division, the appellant observed that the patent was filed in 1997 and that the proceedings before the first instance, in particular the examination, required a long time. In order to avoid any further procedural delay before reaching a final decision, a remittal to the first instance was to be avoided.

X. In its written submissions, the respondent argued that the appellant had the burden of proving that the controlled-release formulations defined in claim 1 of the main request (previous auxiliary request 1) were different from the formulations of D1 in view of the process features recited in the claim. There were no data showing that formulations obtained by processes of hot-melt extrusion, carried out under different conditions, were always different from the formulations of D1. The declarations of documents D8 and D9 referred to ethylcellulose-based formulations. However, the formulations of the patent in suit contained high molecular weight poly(ethylene oxide) which was not comparable to ethylcellulose. Furthermore, in the

assessment of novelty, not only the examples, but the whole disclosure of the prior art document was to be considered. In D1 it was indicated that one of the methods for preparing the formulations was by extrusion molding. Claim 1 of auxiliary request 1 was therefore not novel.

XI. The appellant requested that the decision under appeal be set aside and the patent maintained on the basis of the of the new main request (filed with the grounds of appeal on 30 April 2012 as auxiliary request 1) or, in the alternative, on the basis of the claims filed with the grounds of appeal as auxiliary requests 2, 3, 4 or 5.

XII. The respondent requested in writing that the appeal be dismissed or, in case the Board should conclude that any of the appellant's requests complied with the requirements of sufficiency of disclosure and novelty, that the case be remitted to the Opposition Division for consideration of the issue of inventive step.

Reasons for the Decision

Main Request (set of claims submitted on 30 April 2012 as auxiliary request 1)

1. Sufficiency of disclosure

During the appeal stage the respondent did not submit any argument in relation to this ground of opposition. The Board sees no reasons to deviate from the decision of the opposition division that the requirement of sufficiency of disclosure is met.

2. Novelty

2.1 Document D1 discloses in Table 4 four compositions containing acetaminophen as active ingredient and as excipients the commercial products POLYOX303 and PEG6000, wherein the amount of PEG6000 does not exceed the amount of POLYOX303. POLYOX303 is a poly(ethylene oxide) polymer with an average molecular weight of $7X10^6$ (see page 4, line 36) and falls therefore within the definition of high molecular weight poly(ethylene oxide) of claim 1. PEG6000 is a poly(ethylene glycol) polymer with an average molecular weight of 6000. As acknowledged by both parties, poly(ethylene glycol) is a polymer consisting of ethylene oxide units.

2.2 The formulations disclosed in the examples of D1 are prepared by a process of compression molding. In the description of D1, reference is made also to the technique of extrusion molding (page 13, line 22). However, in the Board's opinion, D1 fails to provide a disclosure of a formulation having the composition defined in claim 1 of the main request which has been prepared by a process of extrusion molding.

2.3 In order to decide on the novelty of claim 1 it needs to be investigated whether the hot-melt extrusion process used in the patent in suit results in the preparation of formulations which are different from the formulations obtained in D1 by a compression molding process.

2.4 Both Dr Zeng and Dr Manning affirm in their declarations (documents D8 and D9) that products formed by hot-melt extrusion have different properties than products formed by compression. In particular, the two experts concur in concluding that products formed by

methods of compression are heterogenous solids consisting of individual drug and excipient particles in random spatial order. On the other hand, products formed by hot-melt extrusion are more homogenous to the point that they can be defined as "solid solution" (see D8 paragraphs 39 to 42 and D9 paragraphs 77 to 80).

The Board notes that the observations of both experts relate in general terms to formulations obtained by processes of hot-melt extrusion without any restriction as to the components of the formulations or the operative conditions adopted for their preparation (e.g. specific range of temperature).

2.5 Evidence of the different properties of tablets obtained by compression or hot-melt extrusion is provided in Exhibit F of D8. This document relates to an experimental study carried out with guaifenesin tablets containing ethyl cellulose as excipient. The tablets have been prepared by compression or by hot-melt extrusion. The data disclosed in figure 1 (page 514) show that the drug release of tablets prepared by hot-melt extrusion is considerably slower than the drug release of tablets prepared by compression.

The respondent observes that while the formulations tested in Exhibit F of D8 contain ethyl cellulose as excipient, claim 1 in suit relates to compositions containing poly(ethylene oxide). In this respect it is noted, however, that on page 510 of this document (see first full paragraph) it is underlined that several researchers have suggested that controlled-release dosage forms prepared by hot-melt extrusion have slower release rates than dosage forms prepared by traditional methods. Hence, the observations based on experiments carried out with compositions containing ethyl

cellulose as excipient appear to confirm a general behaviour of the formulations prepared by hot-melt extrusion which does not depend on the specific polymers used as excipient.

2.6 The unique properties of controlled-release formulations prepared by hot-melt extrusion are confirmed by document D10 in which it is stated that hot-melt extruded dosage forms can be distinguished from conventional dosage forms due to the morphological orientation caused by the extrusion process (see [0062]).

2.7 In view of the above, the Board considers that the hot-melt extrusion process used for preparing the controlled-release formulations of claim 1 render these formulations different from those disclosed in D1, which have been prepared by a process of compression molding.

The subject-matter of the main request therefore complies with the requirement of novelty.

Remittal

3. The essential function of an appeal is to consider whether the decision issued by the first-instance department is correct. Hence, a case is normally remitted to the first-instance department if essential questions regarding the patentability of the claimed subject-matter have not been examined and decided by that department.

3.1 In particular, remittal is considered by the Boards in cases where a first-instance department issues a decision against a party solely upon a particular issue

which is decisive for the case, and leaves other essential issues outstanding. If, following appeal proceedings, the appeal on the particular issue is allowed, the case is normally remitted to the first-instance department for consideration of the undecided issues (Article 111(1) EPC).

3.2 The observations made above fully apply to the present case. The patent was revoked for lack of novelty in view of document D1, without any assessment of the requirement of inventive step. Moreover, document D1, which is the sole prior art document discussed in the appealed decision, does not relate to pharmaceutical compositions prepared by hot-melt extrusion. Since the main issue addressed by the patent is the provision of controlled-release formulations prepared by hot-melt extrusion, document D1 does not appear to be a highly relevant document for the assessment of inventive step.

Hence, the assessment of this requirement would be based on prior art documents which were not considered at all in the appealed decision.

3.3 While the respondent requested in its submissions of 12 October 2015 to remit the case to the opposition division if one of the requests were considered to comply with the requirement of novelty, the appellant requested during oral proceedings to avoid a remittal in consideration of the fact that the proceedings, in particular the examination, had already been very long.

3.4 The Board considers that the appellant's arguments do not affect the validity of the considerations put forward in point 3.2 above. Moreover, the appellant itself contributed to the long duration of the examination proceedings by requesting several

time-extensions to reply to the communications of the examining division.

3.5 Under these circumstances, the Board, in the exercise of its discretionary power pursuant to Article 111(1) EPC, finds it appropriate to remit the case on the basis of the main request to the opposition division for further prosecution.

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 for further prosecution.

The Registrar: The Chairman:

N. Schneider J. Riolo

Decision electronically authenticated