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Datasheet for the decision of 28 September 2017

Case Number: T 1694/15 - 3.3.07

Application Number: 09425135.2

Publication Number: 2238974

IPC: A61K9/20, A61K9/16

Language of the proceedings: EN

Title of invention:
Granulate for the formulation of orodispersible tablets

Patent Proprietor:
E-Pharma Trento S.p.A.

Opponent:
Alpex Pharma S.A.

Headword:
Granulate for tablets/E-Pharma

Relevant legal provisions:
EPC Art. 100(b), 56

Keyword:
Insufficiency of disclosure (no)
Inventive step - (yes)

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Case Number: T 1694/15 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 28 September 2017

Appellant: (Opponent)	Alpex Pharma S.A. Via Cantonale 6805 Mezzovico (Lugano) (CH)
Representative:	Longoni, Alessandra AL & Partners Srl Via C. Colombo ang. Via Appiani (Corte del Colone) 20831 Seregno (MB) (IT)
Respondent: (Patent Proprietor)	E-Pharma Trento S.p.A. Via Provina, 2 Frazione Ravina 38123 Trento (IT)
Representative:	Allaix, Roberto PGA S.p.A. Via Mascheroni, 31 20145 Milano (IT)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 29 June 2015 rejecting the opposition filed against European patent No. 2238974 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	D. Boulois
Members:	A. Usuelli
	Y. Podbielski

Summary of Facts and Submissions

I. European patent No. 2 238 974, based on European patent application No. 09425135.2, was granted on the basis of 17 claims.

Independent claims 1, 7, and 11 of the patent read as follows:

"1. A granulate comprising a mixture of mannitol and sorbitol in a ratio by weight of between 70:30 and 97:3, said granulate having a residual moisture content of less than 0.20% by weight relative to the weight of the same granulate, obtained after granulating by introducing air at a temperature below 80°C with a moisture content of less than 5000 ppm for less than 30 minutes."

"7. An orodispersible tablet comprising at least one active ingredient dispersed in a granulate according to claim 1."

"11. A process for the production of a granulate comprising mannitol and sorbitol, the said process comprising the following steps:
(i) providing mannitol and sorbitol in the form of powder,
(ii) providing a mixture of the said mannitol and the said sorbitol in a ratio by weight of between 70:30 and 97:3,
(iii) introducing the said mixture into a fluidised bed granulator,
(iv) granulating the said mixture under the following conditions:

(a) spraying a quantity of water of between 5% and 35% by weight with respect to the weight of the said mixture, and
(b) introducing air at a temperature below 80°C with a moisture content of less than 5000 ppm, for less than 30 minutes
so obtaining a granulate having a residual moisture content of less than 0.20% by weight relative to the weight of the same granulate."

II. The patent was opposed on the ground that its subject-matter lacked inventive step and it was not sufficiently disclosed. The following document was among those cited during the opposition proceedings:

D2: US 5,576,014

III. By decision posted on 29 June 2015 the opposition division rejected the opposition.

According to the decision under appeal:

(a) The skilled person would have been able to prepare the granulate defined in claim 1 of the patent with a residual content of less than 0.20%. The requirement of sufficiency of disclosure was therefore met.

(b) Document D2 was the closest prior art for the assessment of inventive step. The composition defined in claim 1 of the patent differed from the composition of D2 in the requirement that the residual moisture content was less than 0.20%. This had the effect of improving the hardness properties of the tablets. Since the prior art did not suggest that the hardness properties of a tablet could be

improved by providing a granulate with a moisture content of less than 0.20% the requirement of Article 56 EPC was met.

IV. The opponent (hereinafter: the appellant) lodged an appeal against that decision.

V. Oral proceedings were held on 28 September 2017. They were not attended by the appellant as announced in advance in its letter of 5 September 2017.

VI. In relation to the requirement of sufficiency of disclosure the appellant in its written submission essentially argued that the skilled person could not know without undue burden how to prepare a granulate with a moisture content of less than 0.20% as required by claim 1. It furthermore remarked that no information was given in the patent on how to adjust the granulation parameters when the ratio mannitol to sorbitol was different from 9:1, i.e. the ratio used in the examples of the patent.

As to inventive step, the appellant argued starting from D2 as the closest prior art. This document suggested in column 13, lines 26 to 31 to work on the moisture content of the granulate in order to improve the hardness of the tablets. Inventive merit should have been proved by showing an improvement over D2. However, no comparative example was disclosed in the patent. The requirements of inventive step was therefore not met.

VII. The patent proprietor (hereinafter: the respondent) observed that the examples and the comparative examples of the patent gave enough guidance on how the process parameters could be optimised in order to obtain a

granulate with a residual moisture content of less than 0.20%. The requirement of sufficiency of disclosure was therefore met.

Concerning inventive step, the respondent essentially argued that D2 did not indicate that the technical problem of providing a tablet with optimum hardness properties could be solved by reducing the moisture content of the granulate below 0.20%. In this respect, the passage of column 13 of D2 referred to by the appellant was not relevant since it related to operations to be carried out after compression of the granulate, i.e. on the final tablet. The patent was therefore inventive.

VIII. The appellant requested that the decision under appeal be set aside and that the patent be revoked.

IX. The respondent requested that the appeal be dismissed.

Reasons for the Decision

PATENT AS GRANTED

1. Sufficiency of disclosure

1.1 The appellant's main objection concerns the feature of independent claims 1 and 11 defining the residual moisture content of the granulate. In its opinion, the skilled person would not be able to achieve a moisture content of less than 0.20% without undue burden.

1.2 The Board notes that the description of the patent provides in paragraphs [0039] to [0045] some general information concerning the preparation of the granulate of claim 1. Furthermore, example 3 (to be considered in

combination with paragraph [0071]) discloses a granulate having a moisture content below 0.20% which is prepared by a process according to claim 11 (see second entry of Table 4).

The description teaches that the moisture content of the granulate depends primarily on the drying temperature, the drying time and the relative humidity of the air introduced into the fluidised bed granulator. Paragraph [0044] and table 4 provide guidance on how these parameters should be adjusted in order to achieve the desired moisture content. In this respect the Board considers that the skilled person could derive useful information not only from example 3 (see above) but also from the comparative examples. For instance, the third entry of Table 4 shows that when the granulation is carried out at a drying temperature of 50°C and the relative humidity of the air is 0.1%, the granulate has a moisture content of 0.25%, i.e. slightly above the threshold of claim 1. The skilled person would therefore learn that if the drying temperature should not exceed 50°C then the relative humidity of the air introduced into the fluidised bed granulator should be below 0.1%.

Hence, in the Board's view the skilled person would be able to adjust the relevant process conditions in order to obtain a moisture content less than 0.20%.

1.3 The appellant has furthermore remarked that no information is given in the patent on how to adjust the granulation parameters when the ratio mannitol to sorbitol is different from 9:1, i.e. the ratio of the examples of the patent. However, it did not submit any evidence or technical argument to show that some unsurmountable difficulties could arise when the ratio

mannitol to sorbitol is not 9:1. The Board sees therefore no reason to consider that the skilled person would not be able to carry out the invention over the whole mannitol to sorbitol ratio range defined in the claims (i.e. 70:30 to 97:3).

1.4 In view of the above considerations the Board concludes that the patent meets the requirement of sufficiency of disclosure.

2. Inventive step

The invention underlying the patent in suit relates to a granulate for the formulation of orodispersible tablets (paragraph [0001]).

2.1 Closest prior art

The Board has no reason to diverge from the common position of the parties regarding the choice of document D2 as the closest prior art.

Example 3 of D2 (see also reference to example 1) describes the preparation of a granulate comprising sorbitol and mannitol by the use of a fluidised bed granulator. According to the respondent's calculation, which was not contested by the appellant, the mannitol to sorbitol ratio of the granulate prepared in this example is 95.24 : 4.76, i.e. within the range of claim 1 of the patent in suit.

No information is given in example 3 or in any other part of D2, as to the residual moisture content of the granulate. In the Board's opinion the teaching of D2 strongly indicates that the moisture content of the granulate of example 3 is higher than 0.2%. In this

respect it is noted that no indication is given in D2 as to the importance of producing a granulate having a low moisture content. Quite to the contrary, the low temperature of the drying air (20°C to 30°C, see column 13, lines 7 to 11) and the absence of any restriction as to its moisture content suggest that it was not an objective of the inventors of D2 to produce a granulate containing small amounts of residual water. Indeed, the process disclosed in example 1 of D2, which is used also for the preparation of the granulate of example 3, involves the dissolution of the saccharides in relatively high amounts of water (180 g of water per 420 g of saccharides, i.e. around 43% by weight with respect to the weight of the saccharides). In contrast thereto, in the process described in the patent in suit mannitol and sorbitol are mixed in powder form and then a limited amount of water is sprayed during the granulation (in example 1 around 20% by weight with respect to the weight of the mixture of mannitol and sorbitol).

Thus, the Board agrees with the conclusion of the opposition division that granulate defined in claim 1 of the patent in suit differs from the granulate disclosed in example 3 of D2 in that the residual moisture content is less than 0.20%. This conclusion was not disputed by the parties.

2.2 Technical problem

2.2.1 Table 6 of example 4 of the patent discloses the hardness of tablets 6 to 8 prepared from granulates having different residual moisture contents. According to the evaluation reported in paragraph [0079], tablet 6, prepared from granulate F with residual moisture content of 0.11%, has an optimal hardness. Tablets 7

and 8 are comparatives tablets since they are prepared from granulates having a residual moisture content higher than 0.20%. Tablet 7, prepared from granulate G with residual moisture content of 0.26%, shows an increased hardness which negatively affects its disintegration in the mouth. Tablet 8, prepared from granulate H with residual moisture content of 0.78%, has a too rapid degradation.

2.2.2 The appellant observes that this comparative experiment is not based on a comparison with the product of example 3 of D2. The Board agrees with this. It is nevertheless noted that the experiment disclosed in example 4 is based on a comparison of granulates having different residual moisture contents. It is therefore relevant for the definition of the technical problem in that it makes it possible to assess the effects of the distinguishing feature over D2, i.e. the selection of a residual moisture content of less than 0.20%.

2.2.3 On the basis of the data disclosed in the patent, the technical problem can be defined as the provision a granulate that makes it possible to prepare tablets with optimal hardness.

2.3 Obviousness

2.3.1 Document D2 does not establish any link between residual moisture content of the granulate and hardness of the tablets. Thus, a skilled person facing the problem defined in 2.2.3 above would have no reason on the basis of the teaching of D2 to work on the residual moisture content of the granulate.

2.3.2 The appellant refers to the passage of column 13 of D2 (lines 26-31) indicating that *"the hardness of the tablet after tabletting can be further improved...by appropriately utilizing the step comprising spraying a physiologically acceptable organic solvent or water, and drying; a step comprising humidity treatment and drying; or the like"*. In its opinion, in the light of this passage the skilled person would have been strongly suggested to dry the granulate in order to improve the hardness of the tablet.

However, as observed by the respondent, this passage of D2 relates to process steps which are to be carried out "after tabletting", i.e. after compression of the granulate. Thus, it does not teach to reduce the moisture content of the granulate in order to improve the hardness properties of the tablets.

2.3.3 It follows from the above, that the subject-matter of claim 1 meets the requirements of Article 56 EPC.

2.4 Independent claim 7 is also inventive since it relates to tablets containing the granulate of claim 1. Process claim 11 does not contain any explicit reference to claim 1. However, the process relates to the preparation of a granulate having the same composition and the same moisture content of the granulate of claim 1. Thus, the considerations set out above in relation to claim 1 apply also to claim 11. Accordingly, claim 11 meets the requirements of Article 56 EPC as well.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

S. Fabiani D. Boulois

Decision electronically authenticated