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**Datasheet for the decision
of 15 January 2016**

Case Number: T 1736/12 - 3.3.07

Application Number: 02727770.6

Publication Number: 1392247

IPC: A61K9/16

Language of the proceedings: EN

Title of invention:

PROCESS FOR PREPARING GRANULAR COMPOSITIONS

Applicant:

Reckitt Benckiser Healthcare (UK) Limited

Relevant legal provisions:

EPC Art. 56
RPBA Art. 13(1), 13(3)

Keyword:

Requests submitted during oral proceedings - admitted (yes)
Inventive step - main request and auxiliary request (no)



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Chambres de recours**

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Case Number: T 1736/12 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 15 January 2016

Appellant: Reckitt Benckiser Healthcare (UK) Limited
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 22 February
2012 refusing European patent application
No 02727770.6 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman J. Riolo
Members: A. Usuelli
I. Beckedorf

Summary of Facts and Submissions

I. The appeal of the applicant (appellant) lies from the decision of the examining division announced at the oral proceedings held on 7 December 2011 to refuse European patent application No. 02727770.6.

II. The documents cited during the examination proceedings included the following:

D2: US 5,667,807

D5: US 6,150,424

D6: EP 665009

D7: WO 97/18839

III. The decision was based on two sets of claims filed on 7 November 2011 as main request and auxiliary request.

Claim 1 of both requests related to a process for the preparation of a granular composition comprising a non-steroidal anti-inflammatory drug (NSAID).

Claim 1 of the main request, which is still relevant in the context of the present decision, read as follows:

"1. A process for the preparation of a granular composition comprising solidified melt granules comprising a non-steroidal anti-inflammatory drug (NSAID) as a continuous phase, which process comprising the steps of:

(a) melt-extruding the NSAID, optionally with excipients;

(b) forming a homogeneous extrudate;

(c) cooling the extrudate; and

(d) comminuting the cooled extrudate to form granules; characterised in that in step (a) the NSAID is fully

melted and that the NSAID and optional excipients are heated to a temperature of 80 - 130°C, and that in step (b) the extrudate is formed into two or more ribbons having a depth of 10 mm or less and which solidify in 5 minute or less."

Both requests also included independent claims directed to an apparatus suitable for use in the process of claim 1.

IV. According to the decision under appeal, document D5 was the closest prior art for the subject-matter of the main request. The process for preparing a composition comprising ibuprofen disclosed therein differed from the process of claim 1 in that no mention was made of multiple extruded ribbons which solidified quickly. The technical problem in view of document D5 was seen in the provision of a method to increase the output of the process of production of extrudate comprising an NSAID. Document D2 described a process for thermal granulation in which the NSAID was extruded into multiple strands. The skilled person would have combined the teachings of D5 and D2, thereby arriving at the solution of providing a plurality of thin strands. The process of claims 1 to 22 was therefore obvious. Claims 23 to 27 relating to an apparatus for carrying out the process of claim 1 were also not inventive.

The same line of argumentation as that followed for the main request applied also to the subject-matter of the auxiliary request.

In addition, the auxiliary request was considered to lack inventive step also when starting from document D2 as the closest prior art. The process of claim 1 differed from the process of D2 mainly in that the

NSAID was fully melted. The technical problem in view of document D2 was seen in the provision of a process for the production of NSAID with convenient dissolution properties. Examples 3 and 4 of document D6 disclosed a process in which the NSAID indomethacin was fully melted. The subject-matter of the auxiliary request was obvious in view of the combination of the teachings of documents D2 and D6.

- V. The appellant lodged an appeal against that decision. With the statement setting out the grounds of appeal, sent on 22 June 2012, the appellant submitted a main request and two auxiliary requests.

- VI. In a communication dated 12 October 2015 issued in preparation for oral proceedings, the Board expressed the opinion that the subject-matter of claim 1 of all the requests was obvious starting from document D2 as the closest prior art, while the independent claims of all the requests concerning an apparatus suitable for use in the process of claim 1 were obvious in the light of the teaching of D7.

- VII. In the course of the oral proceedings held on 15 January 2016 the appellant submitted four new requests and withdrew the requests filed with the statement setting out the grounds of appeal.

After a discussion on the admissibility of the new requests, the appellant stated that it was maintaining only two of them, as main request and first auxiliary request.

These requests were based on the main request and first auxiliary request submitted with the statement setting

out the grounds of appeal and differed therefrom mainly in the deletion of the apparatus claims.

Claim 1 of the main request was identical to claim 1 of the main request forming the basis of the decision of the examining division (see point III above).

Claim 1 of the first auxiliary request differed from claim 1 of the main request in specifying that in each ribbon of molten extrudate the width was greater than the depth.

VIII. In the statement setting out the grounds of appeal the appellant considered document D5 as the closest prior art. However, during the oral proceedings it eventually submitted its arguments on inventive step starting from document D2 as the closest prior art. It remarked that the process according to claim 1 of both requests differed from the process of D2 in that the NSAID was fully melted while in the process of D2 only a partial melting occurred. Moreover, in the example of D2 the extrudate was cooled in the air. This method was lengthy, while according to the process of the application in suit the extrudate solidified in less than 5 minutes. The product prepared according to the process of the invention had better dissolution properties, as explained on page 3 of the description. Furthermore, Figure 7 of the application in suit showed that it was also more stable. The prior-art documents did not suggest modifying the process of D2 by carrying out the melt-extrusion under conditions in which the NSAID was fully melted. Document D5 would not have been considered by the skilled person since it related to a particular technology for foaming pharmaceutical compositions which was not relevant to the invention of

the application in suit. The subject-matter of both requests was therefore inventive.

- IX. The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of one of the sets of claims filed as main request and first auxiliary request during the oral proceedings.

Reasons for the Decision

1. *Admittance of the main request and first auxiliary request*

Both the main request and first auxiliary request were submitted during the oral proceedings. They are based respectively on the main request and first auxiliary request submitted with the statement setting out the grounds of appeal, and differ therefrom mainly in the deletion of the claims relating to an apparatus suitable for use in the process of claim 1.

Hence, the new requests do not raise any new issue and can be regarded as a response to the negative opinion expressed by the Board in its communication of 12 October 2015 regarding inventive step of the apparatus claims (see point VI).

In view of the above, the Board in the exercise of its discretion decides to admit the main request and the first auxiliary request into the appeal proceedings (Article 13(1) and (3) RPBA).

2. *Main request - Inventive step*

The invention underlying the application in suit relates to a process for the preparation of a granular composition containing a non-steroidal anti-inflammatory drug (NSAID) which includes a step in which the active ingredient is melt-extruded.

2.1 Closest prior art

- 2.1.1 Document D2 relates to a process for the production of granules containing an active ingredient having a melting point between 40°C and 150°C (see claim 1). The four examples of this document disclose the preparation of granules containing ibuprofen or ketoprofen, i.e. NSAIDs. The process involves a step of melt-extrusion of a mixture of the active ingredient with excipients (see claim 1).

The Board considers this document to represent the closest prior art for the assessment of inventive step. This was agreed by the appellant during the oral proceedings (see point VIII above).

- 2.1.2 The process of document D2 comprises a step in which the active ingredient and the excipients are mixed and added to a heatable extruder (column 2, lines 19 to 21). The mixture is compacted to obtain an extrudate at a temperature at which part of the active ingredient is melted (column 2, line 24). The extrudate is pressed through a perforated plate to give thin homogenous strands of 0.3-2.0 mm which are comminuted after cooling to provide the granules (column 2, lines 25 to 27 and example 1).

The strands of 0.3-2.0 mm referred to in D2 are not distinguishable from the "ribbons" having a depth of 10 mm or less recited in claim 1.

Thus, the process of claim 1 of the application in suit differs from the process of D2 mainly in that the NSAID is fully melted while in D2 it is only partially melted.

2.2 Technical problem

2.2.1 In the second paragraph of page 3 of the description it is stated that by heating the NSAID to a temperature above its melting point further processing advantages and formulation advantages are obtained. During the oral proceedings the appellant underlined in particular the better stability and dissolution profile of the granules prepared according to the process of the invention. Further advantages over the process of D2 were associated with the rapid cooling of the extrudate.

2.2.2 As pointed out also in the decision under appeal (page 5, fourth full paragraph), the application does not contain any experimental data based on a comparison between the process of the invention and the process of D2.

2.2.3 Figure 7 of the application in suit, referred to by the appellant during the oral proceedings, relates to a comparative stability study which is briefly described in example 27. The tablets compared with the formulations obtained according to the process of the invention are simply defined as "ibuprofen tablets containing standard starch based granules". As observed by the appellant, example 1 of D2 discloses the

preparation of ibuprofen tablets containing starch. However, example 27 of the application in suit does not contain any reference to document D2. Furthermore, no information is given in this example, or in any other part of the application, as to the exact composition of the comparative tablets and as to the method for their preparation. It is not even clear whether these tablets are prepared in a process involving a step of melt-extrusion. Thus, it cannot be assumed that the comparative compositions tested in example 27 represent the teaching of D2.

Similar considerations apply to the composition representing the subject-matter of the application in suit. The information provided in example 27 with regard to this composition is limited to the indication that it contains ibuprofen. It is however unclear whether this composition contains the same excipient of the comparative compositions, i.e. starch, or whether a different excipient has been used. In this respect the Board observes that none of the compositions prepared in the examples of the application in suit contains starch.

Accordingly, the data of Figure 7 cannot be taken as a basis for comparing the stability of the tablets prepared according to the process of claim 1 and the tablets of D2.

- 2.2.4 Concerning the alleged advantages deriving from the rapid cooling of the extrudate, the Board observes that the application does not provide any data about them. Nor has the appellant submitted any corroborating evidence during the proceedings. There is also no evidence of a more rapid solidification for the extrudate of the invention than for the extrudate

obtained in D2. In this respect the Board observes that D2 does not require any restriction as to the methods for cooling the extrudate. Furthermore, since the process of D2 does not require a complete melt of the active ingredient it can be carried out at lower temperatures. The extrusion temperature in examples 1 to 3 of D2 is indeed much lower than the temperature of the extruded material in the examples of the application.

- 2.2.5 Also in respect of the dissolution properties, no data are available which make possible a comparison with the tablets of D2.

However, the Board notes that on page 5 of the description it is explained that the crystalline structure of the melt granules formed from solidifying a fully melted NSAID differs from the crystalline structure where the NSAID is only partially melted. In the latter the crystalline structure of the melted NSAID is interrupted by the crystals of the non-melted NSAID. In contrast, in the case of complete melting, a single continuous phase of the NSAID is formed.

Although this observation is not corroborated by any evidence, the Board regards it as plausible and sees no reasons to question it.

In the light of this explanation the Board considers it also credible that the tablets prepared according to the process of the application in suit have an improved dissolution profile over the tablets of D2. This conclusion is based on the general knowledge that different crystalline forms of the same substance may have different dissolution properties. Hence, a single continuous crystalline phase very likely dissolves in a

more homogeneous manner than a composition made of different crystalline forms of the NSAID.

2.2.6 In view of the above, the technical problem can be formulated as the provision of a melt-extrusion process for preparing a granular composition of an NSAID having an improved dissolution profile.

2.3 Obviousness

It follows from the considerations set out above in relation to the definition of the technical problem (see point 2.2.5) that the skilled person, based on his general knowledge, would know that a composition consisting of a single crystalline phase would have a more homogeneous dissolution profile than a composition containing different crystalline forms of the active ingredient. Hence, faced with the problem of improving the dissolution properties of the compositions obtained in D2, he would modify the step of partial melting into a step in which the NSAID is fully melted, in order to prevent the formation of different crystalline forms.

In this respect the Board also observes that melt-extrusion processes involving the complete melt of the NSAID were already known before the priority date of the patent. For instance, the processes of examples 1 and 2 of D5 are carried out at a temperature of 150°C, which is well above the melting point of the active ingredient, i.e. ibuprofen (melting point 75-77°C according to the description of the present application). Hence, the skilled person would have had no doubt as to the feasibility of a process involving the complete melt of an NSAID.

Consequently, the subject-matter of the main request does not involve an inventive step.

3. *First auxiliary request - Inventive step*

3.1 Claim 1 of this request differs from claim 1 of the main request in the requirement that the width of each ribbon of molten extrudate is greater than the depth.

3.2 The appellant did not claim any specific advantage or surprising property deriving from this feature. In the description of the application (page 10, lines 15 and 16) it is explained that in order to optimise the cooling of the extrudate ribbons, these should have a width which is greater than the depth.

3.3 The Board considers that it would be evident to the skilled person that ribbons with reduced depth would solidify more rapidly than thick ribbons. It would therefore be obvious to provide the apparatus for the melt-extrusion with channels capable of forming ribbons of extrudate which are more wider than they are deep. This teaching can be derived also from document D2, which indicates that the extruded material should have the form of thin strands.

In view of the above, the Board considers that the feature concerning the shape of the ribbons does not make any inventive contribution to the subject-matter of claim 1.

Consequently the subject-matter of the first auxiliary request does not meet the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed

The Registrar:

The Chairman:



S. Fabiani

J. Riolo

Decision electronically authenticated