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D E C I S I O N
of 13 October 2005

Case Number: T 0436/03 - 3.3.02

Application Number: 95913091.5

Publication Number: 0750492

IPC: A61K /9

Language of the proceedings: EN

Title of invention:

Inhalation composition containing lactose pellets

Patentee:

Glaxo Group Ltd.

Opponent:

Schering Corp.

Headword:

Inhalation composition/GLAXO GROUP

Relevant legal provisions:

EPC Art. 54, 123(2)

Keyword:

"Main request; Novelty (no): the prior art discloses clearly and unambiguously the disputed feature"

"Auxiliary requests 1 to 5: Requirements of Article 123(2) have not been met"

Decisions cited:

T 0666/89, T 0198/84

Catchword:

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Case Number: T 0436/03 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 13 October 2005

Appellant: Glaxo Group Ltd
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Respondent: Schering Corp.
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 5 March 2003
revoking European patent No. 0750492 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: M. C. Ortega Plaza
P. Mühlens

Summary of Facts and Submissions

- I. European patent No. EP-B-0 750 492, based on application No. 95 913 091.5 (in turn based on international patent application WO 95/24889), was granted on the basis of 15 claims.

Independent claim 1 as granted read as follows:

"1. A pharmaceutical powder composition suitable for inhalation comprising microfine particles of medicament and at least one lactose pellet having a diameter of from 10 to 1500 micrometers, which pellet comprises a plurality of lactose particles, of which at least 90% by weight have a diameter of less than 15µm."

Independent claim 12 as granted read as follows:

"12. A process for preparing a pharmaceutical composition according to any preceding claim, comprising admixing microfine particles of medicament with at least one lactose pellet having a diameter of from 10 to 1500 micrometers, which pellet comprises a plurality of microfine lactose particles."

Independent claim 14 as granted read as follows:

"14. An inhalation device comprising a compound [*sic*] according to any one of claims 1 to 11."

- II. For the present decision the following document has been taken into consideration:

(1) US-A-5 143 126

III. Opposition was filed and revocation of the patent in its entirety was requested pursuant to Article 100(a) EPC on the grounds of lack of novelty and lack of inventive step and pursuant to Article 100(b) EPC on the grounds of insufficiency of disclosure.

IV. The appeal lies from the decision of the opposition division revoking the patent under Article 102(1) EPC.

The opposition division considered that the requirements of sufficiency of disclosure (Article 83 EPC) were met by the patent in suit since the description disclosed several embodiments covering the subject-matter of claim 1 and it contained general information for performing the claimed invention.

The opposition division considered that the claim wording merely required the presence of at least one lactose pellet, whereas all other pellets, if any, could be there without meeting the requirements set out in the claim for the individual pellet, as long as the composition remained suitable for inhalation. Furthermore, the claim did not specify as a feature that the pellet had to break apart into particles during use.

In the opposition division's view, claim 1 also encompassed compositions where microfine medicament particles were separate from the -at least one- lactose pellet, including in or on the pellet microfine medicament particles.

The opposition division considered that the subject-matter claimed in claim 1 of the main request lacked novelty over the contents of document (1). Basically, the opposition division found that document (1) disclosed compositions suitable for powder inhalation, comprising microfine medicament particles and lactose pellets having an average diameter of 50 to 2000 μm , which were formed from formoterol particles and lactose particles having an average particle size of less than 50 μm , preferably from 1 to 10 μm . The opposition division further considered that the compositions of document (1) necessarily comprised at least one lactose pellet having a diameter of from 10-1500 μm , comprising particles of below 15 μm in view of the preferred average particle size values listed in the description of document (1).

According to the opposition division's findings, the first auxiliary request met the requirements of Articles 123 and 54 EPC. Novelty was established in view of the specified water content of the pellet. However, the opposition division considered that the subject-matter of the first auxiliary request lacked an inventive step vis-à-vis document (1) since the fact that one single pellet had a certain water content was immaterial when defining the problem to be solved.

As regards the second auxiliary request, the opposition division considered that it met the requirements of Articles 123, 84 and 54 EPC, but it lacked an inventive step vis-à-vis document (1) since the choice of a multi-dose reservoir device was arbitrary.

The opposition division also stated that auxiliary requests 3 to 6 were withdrawn during the oral proceedings and considered that the late-filed auxiliary request 7 was not admissible.

- V. The patentee (appellant) lodged an appeal against said decision and filed grounds of appeal.
- VI. The appellant filed a main request with its letter of 12 June 2003 and six auxiliary requests.

Claim 1 of the main request is identical to claim 1 as granted.

- VII. A communication from the board was sent as an annex to the invitation to the oral proceedings.
- VIII. The appellant filed five auxiliary requests with its letter of 7 September 2005. It maintained its main request and withdrew the six auxiliary requests filed with its letter of 12 June 2003.

The five auxiliary requests filed with the appellant's letter of 7 September 2005 have been renumbered as auxiliary requests 1 to 5.

Claim 1 of the first auxiliary request read:

"1. A pharmaceutical powder composition suitable for inhalation comprising from 0.1% to 90% w/w of microfine particles of medicament and from 10% to 99.9% w/w lactose pellets having a diameter of from 50 to 1000 micrometers, said composition comprising at least one lactose pellet having a diameter of from 10 to 1500

micrometers, which pellet comprises a plurality of lactose particles, of which at least 90% by weight have a diameter of less than 15 μ m."

Claim 1 of the second auxiliary request differs from claim 1 of the first auxiliary request only in the introduction of the following feature at the end of the claim:

", wherein the composition contains less than 1% w/w of unbound water."

Claim 1 of the third auxiliary request read as follows:

"1. A multi-dose reservoir inhaler device having a bulk powder container containing a pharmaceutical powder composition suitable for inhalation; and a metering cavity for metering said pharmaceutical powder composition from said bulk powder container, wherein the pharmaceutical powder composition comprises from 0.1% to 90% w/w of microfine particles of medicament and from 10% to 99.9% w/w lactose pellets having a diameter of from 50 to 1000 micrometers, said composition comprising at least one lactose pellet having a diameter of from 10 to 1500 micrometers, which pellet comprises a plurality of lactose particles, of which at least 90% by weight have a diameter of less than 15 μ m."

Claim 1 of the fourth auxiliary request differs from claim 1 of the third auxiliary request only in the introduction of the following feature at the end of the claim:

", wherein the composition contains less than 1% w/w of unbound water."

Claim 1 of the fifth auxiliary request differs from claim 1 of the first auxiliary request only in that the expression "comprises" after the word "pellet" has been replaced by the expression "consists of".

- IX. Oral proceedings were held before the board on 13 October 2005.
- X. During the oral proceedings, the appellant filed its sixth auxiliary request.

As regards the admissibility of the sixth auxiliary request, the appellant stated that the amendments introduced were clear, simple and easy to handle.

The appellant did not contest the analysis made by the opposition division concerning the wording of claim 1 of the main request. The appellant merely stressed that the case of one single lactose pellet being present in the composition was the extreme case and that, realistically, it would be more than one pellet.

The appellant contested, however, the assessment of novelty made by the opposition division, since the subject-matter claimed in claim 1 was not clearly and unambiguously derivable from the contents of document (1). In the appellant's opinion, the opposition division had erroneously employed criteria concerning inventive step for the assessment of novelty. Furthermore, the opposition division had, when analysing the contents of document (1) (in particular

when interpreting the expression "average diameter"), made use of technical knowledge going beyond the common general knowledge of the skilled person. In this context, the appellant cited decision T 666/89, OJ EPO, 1993, 495.

The appellant stated that document (1) disclosed pharmaceutical compositions sharing the features of the compositions claimed in claim 1 with the exception of the feature concerning the constitution of the lactose pellet, namely: "which pellet comprises a plurality of lactose particles, of which at least 90% by weight have a diameter of less than 15 μ m".

The appellant further argued that document (1) disclosed in column 4, lines 55-58, that the average grain size of the lactose was less than 50 μ m, preferably from 1 μ m to 10 μ m. In the appellant's view there was no pointer in document (1) for making the choice of 1 μ m for the diameter of the particles constituting the pellet.

The appellant stressed that in the field of powder compositions suitable for inhalation there was no such as thing as a "usual average diameter". There were many ways to express the particle size.

In the appellant's view, document (1) dealt with particle processing and particle mixtures which show problems concerning flow. Figures 2a and 2b of document (1) showed respectively the rough (jagged and angular) formoterol and lactose particles prior to processing. Figure 2c of document (1) showed a pellet (rounded, with largely smooth surface) after applying the process disclosed in document (1) to the rough initial

particles. The values appearing in column 4 of document (1) for the average grain size referred to the rough initial particles, but there was no indication in document (1) of the actual size of the particles in the pellets (agglomerated stage).

The appellant also referred to its submissions in a letter of 12 June 2003 in order to demonstrate that only a fairly tight Gaussian distribution would exhibit at least 90% of the particles with a diameter less than 15µm. Therefore, in the appellant's view, one could not take the teaching of document (1), in which pellets were formed by particles having an average diameter of 10µm, as destroying the novelty of the claimed subject-matter.

The appellant argued that there was an incorrect mention of Figure 2c in column 4, line 58 of document (1). This was clear in view of the use of the expression "By contrast" in the next sentence.

The appellant contested the respondent's reading of the particle diameter range appearing in column 4 of document (1) and argued that it referred to average size and not to specific values of individual particles. The appellant argued that this was shown by the fact that the lactose was sifted prior to agglomeration.

The appellant considered that the process according to document (1) was a rather aggressive manufacturing process and hence it could not be assumed that the initial particle sizes also applied to the end particles.

With respect to the basis in the description as originally filed for the feature "from 10% to 99.9% w/w lactose pellets having a diameter of from 50 to 1000 micrometers" appearing in claim 1 of all the auxiliary requests 1 to 5, the appellant mentioned page 3, lines 16-17. It stated that nothing in that sentence related to a particular process.

XI. The respondent contested the admissibility of the sixth auxiliary request on the grounds that it was late filed.

The respondent agreed with the analysis of the wording of claim 1 of the main request made by the opposition division. It also fully agreed with the assessment of novelty of claim 1 of the main request made by the opposition division. In the respondent's opinion, document (1) anticipated the subject-matter of claim 1 of the main request.

The respondent stressed that document (1) concerned the two aspects relating to device and method of using the device for preparing the powder for inhalation.

The respondent argued that the diameter range of "preferably from 1 μ m to 10 μ m", appearing in column 4, was not linked to the word "average". Furthermore, in the respondent's opinion, the appellant's submissions concerning the reading of the passage in column 4 were incorrect.

The respondent submitted that even if the range mentioned referred to the average grain size, there was a situation of overlapping ranges. It cited in this context decision T 198/84, OJ EPO 1985, 209.

As regards the appellant's arguments concerning the size of the particles in the pellet, the respondent stated that the contested patent contained no data concerning the measurement of particle size in the pellet and that the process for preparing the pellet employed in the patent in suit was the same as the process according to document (1). Moreover, when agglomerating by spheronising one would obtain particle sizes even smaller than before processing.

The sifting performed before agglomeration merely introduced a cut in the particle size range 1 μ m to 10 μ m.

The respondent also raised an objection against the novelty of the claimed subject-matter in the light of an additional document which formed part of the art within the meaning of Article 54(3) EPC.

The respondent objected to the sets of claims of auxiliary requests 1 to 5 within the meaning of Articles 123(2) and 84 EPC. Additionally, it objected to the sets of claims of auxiliary requests 3 and 4 within the meaning of Article 123(3) EPC.

- XII. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request filed with letter of 12 June 2003, or, alternatively, on the basis of one of the auxiliary requests 1 to 5 filed with letter of 7 September 2005 or on the basis of the auxiliary request 6 filed in the oral proceedings.

The respondent (opponent) requested that the appeal be dismissed.

Reasons for the decision

1. The appeal is admissible.

2. *Admissibility of the late-filed auxiliary requests*
 - 2.1 The respondent did not contest the admissibility of auxiliary requests 1 to 5 filed with the appellant's letter of 7 September 2005. The board also sees no reason to contest their admissibility since they were a direct response to the comments made in the board's communication sent as an annex to the invitation to the oral proceedings.

 - 2.2 With respect to the admissibility of the set of claims filed during the oral proceedings, the following has been considered:

The sixth auxiliary request is per se late-filed since it was filed by the appellant during the oral proceedings before the board.

The filing of this request during the oral proceedings is not justified since the objections raised and discussed during the oral proceedings concerning the formal requirements of the auxiliary requests filed with the appellant's letter of 7 September 2005 had been known to the appellant from the respondent's letter of 13 September 2005.

Moreover, the amendments introduced in the sixth auxiliary request do not represent a direct response to the objections concerning the main request and discussed in detail during the oral proceedings.

Therefore, the board comes to the conclusion that the set of claims filed during the oral proceedings has to be refused on the grounds of being late filed.

3. *Main request*

3.1 The board agrees with the analysis made by the opposition division concerning the wording of claim 1 of the main request. None of the parties disputed these findings.

3.2 Document (1) discloses an apparatus for agglomerating and metering non-flowable powders and a process for preparing such powders.

Document (1) discloses: "The method and the apparatus according to the invention are especially suitable for metering of very small quantities of a poorly flowable mixture consisting of previously ground and/or sifted lactose and formoterol..." (column 4, lines 40-44)

Document (1) further discloses: "Formoterol is an active ingredient which is used for treating diseases of the human lungs or of the respiratory system, for example asthmatic diseases. The active ingredient is mixed with lactose to form a powder mixture and the powder mixture is inhaled." (column 4, lines 49-53)

Document (1) also states: "The average grain size of the formoterol is approximately 5 μm , and **the average grain size of the lactose is less than 50 μm , preferably from 1 μm to 10 μm .** FIGS. 2a-c show, on a greatly enlarged scale, such formoterol grains **8** (FIG. 2a) and lactose grains **9** (FIG. 2b), the surfaces **81** and **91**, respectively, of which are jagged and angular, which is one of the main causes of the poor flowability of the powder in the non-agglomerated state. By contrast, the surface **101** is substantially rounded, with the result that the pellets **10** are better able to flow." (column 4, lines 55-64) (*emphasis added in the text*).

Furthermore, document (1) discloses: "The average diameter of the pellets **10** is within the range of approximately from 50 μm to 2000 μm , depending on the average grain size of the lactose used, which is sifted prior to agglomeration. The larger the average diameter of the lactose grains **9**, the softer and more unstable the agglomerations. **Especially stable flowable pellets 10 are obtained when formoterol 8 having an average diameter of 5 μm and lactose having an average diameter of 10 μm are used...**" (column 4, lines 67-68 and column 5, lines 1-7) (*emphasis added*).

- 3.3 There was no dispute between the parties that the powder compositions disclosed in document (1) clearly share with the compositions according to claim 1 all the features with the exception of the feature concerning the constitution of the lactose pellet, namely: "which pellet comprises a plurality of lactose particles, of which at least 90% by weight have a diameter of less than 15 μm ".

3.4 As regards the disputed feature, it has to be investigated whether or not it is clearly and unambiguously derivable from the contents of document (1).

The board is convinced that it is probable that the powder composition exemplified in column 5, lines 4-7, of document (1), comprising pellets which are formed from formoterol particles having an average diameter of 5 μm and lactose particles having an average diameter of 10 μm , comprise at least one pellet such as that defined in claim 1. However, probability cannot be used for establishing a lack of novelty.

Therefore, it has to be determined whether it is inevitable that the other pharmaceutical compositions according to document (1) possess such a pellet.

The pharmaceutical compositions disclosed in document (1) comprise pellets which are formed from microfine medicament and lactose particles by tumbling and spheronisation in a process of agglomeration of the initial particles (cf. column 2, lines 27-47).

It becomes apparent from the reading of the passages quoted in point 3.2 above (see especially the last paragraph) that there is a sifting prior to agglomeration which is necessarily performed in order to obtain agglomerates in the form of the pellet 10 shown in FIG. 2c, where the size distribution of the constituting particles has not to be very broadly scattered.

Furthermore, as shown by the passages quoted above (column 4, line 55 and following), it is clearly disclosed in document (1) that the preferred average grain size of the particles of lactose used as starting material is 1 μm to 10 μm . This means, according to the constant jurisprudence of the EPO boards of appeal, that the lower limit value of 1 μm is specifically disclosed for the average grain size of the lactose grains 9 of Fig. 2b which are the particles forming the pellet 10.

Therefore, irrespectively of how this average size of 1 μm is measured for the particles, the pellet 10 necessarily and inevitably comprises a plurality of lactose particles, of which at least 90% by weight have a diameter of less than 15 μm , as required by claim 1.

Accordingly, claim 1 of the main request lacks novelty vis-à-vis the contents of document (1).

3.5 As regards the appellant's argument that the size of the lactose particles undergoing an aggressive manufacturing process such as that disclosed in document (1) would have been modified and hence the initial values for the particles size did not apply to the particles constituting the pellet, the following has been considered:

Apart from the fact that the process disclosed in document (1) is the same as that employed in the patent in suit (cf. paragraph [0015]), the agglomeration taking place during the manufacturing process forms the pellets which comprise the initial particles. The initial particles may have broken their angular edges

and hence may be smaller than the initial particles but not bigger. Furthermore, if they become bigger it is because they form the pellet which is the agglomerated form. Nothing else is required by claim 1 of the main request.

It is also to be noted that the patent in suit does not disclose any measurement of the particle size for the particles in the lactose pellet.

Additionally, the board does not agree with the appellant that the expression "By contrast" appearing in column 4, line 64, of document (1) can be taken as proof that the average grain size appearing in line 58 does not refer to the particles in the pellet 10 of FIG. 2c. The wording mentioned merely reflects the contrast between the surface 101 in the agglomerated and rounded pellet 10 (FIG. 2c) and the surfaces 81 and 91 in the initial rough particles (FIG. 2a and 2b).

Finally, since the size of the medicament particles is defined in claim 1 in a general manner as "microfine particles of medicament", the compositions according to document (1) using initial lactose grains of an average size of 1 μm are encompassed by the claim wording, irrespective of the size of the medicament particles used. Hence, no selection has to take place from the disclosure of document (1) in order to arrive at the subject-matter claimed.

3.6 Consequently, claim 1 of the main request fails for lack of novelty (Article 54(1) and (2) EPC).

3.7 In view of the above conclusions it is unnecessary to establish whether or not the subject-matter claimed is novel over the contents of the additional document cited by the respondent.

4. *Auxiliary requests 1 to 5*

4.1 Claim 1 of all the auxiliary requests 1 to 5 contains the feature which specifies that the pharmaceutical composition comprises "from 10% to 99.9% w/w lactose pellets having a diameter of from 50 to 1000 micrometers".

The appellant cited as the basis for this amendment the following passage on page 6, lines 16-18 of the corresponding application WO 95/24889 (which forms the basis for the application as originally filed):

"Desirably the lactose pellets have a diameter within the range of 50 to 1000 micrometers, particularly 150 to 1000 micrometers, for example in the range of 200 to 800 micrometers."

However, this passage forms part of a paragraph which reads: "For all layering processes it is desirable to restrict the size range of the core pellets and hence it may be advantageous to pass the lactose pellets through one or more sieves to remove over or under-size pellets before layering with medicament." (page 6, lines 13-16, of the corresponding application WO 95/24889).

Therefore, the particle size of the lactose pellets has to be read in its real context as that referring to one of the several alternatives encompassed by the granted

claim, namely the alternative in which the lactose pellets are cover by layer(s) of medicament particles.

This interpretation is confirmed by the next paragraph appearing on page 6 of the corresponding application WO 95/24889, immediately after a space separating it from the previous disclosure concerning the disputed lactose pellet size: "In an alternative embodiment the micronised medicament particles may be pelleted by methods known or analogous to methods known in the art..." (page 6, lines 19-20, of the corresponding application WO 95/24889).

Accordingly, amended claim 1 of all auxiliary requests 1 to 5 contravenes the requirements of Article 123(2) EPC since it relates to a generalisation encompassing all the alternatives from a specific feature disclosed in combination with only one of the alternatives.

- 4.2 Consequently, auxiliary requests 1 to 5 fail because they do not meet the requirements of Article 123(2) EPC.
- 4.3 In view of the circumstances depicted above it is unnecessary to comment on the other objections raised by the respondent concerning the auxiliary requests.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

A. Townend

U. Oswald