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**Datasheet for the decision
of 7 February 2011**

Case Number: T 0106/07 - 3.3.02

Application Number: 97921298.2

Publication Number: 0896525

IPC: A61K 9/12

Language of the proceedings: EN

Title of invention:

Methods of dry powder inhalation

Patentee:

Quadrant Technologies Ltd.

Opponent:

Advanced Inhalation Research Inc
Nektar Therapeutics
Sanofi-Aventis Deutschland GmbH

Headword:

Dry powder inhalation/QUADRANT TECHNOLOGIES INC.

Relevant legal provisions:

EPC Art. 56

Relevant legal provisions (EPC 1973):

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Keyword:

"All requests: inventive step - (no): combination of commonly used parameters for operating a known inhaler"

Decisions cited:

-

Catchword:

-



Case Number: T 0106/07 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 7 February 2011

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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted
15 December 2006 concerning maintenance of
European patent No. 0896525 in amended form.

Composition of the Board:

Chairman: U. Oswald
Members: A. Lindner
L. Bühler

Summary of Facts and Submissions

- I. European patent No. 0 896 525 based on application No. 97 921 298.2 was granted on the basis of 11 claims.
- II. Three oppositions were filed against the patent. The patent was opposed under Article 100(a) EPC for lack of novelty, inventive step and industrial application and for containing matter excluded from patentability under Article 52(4) EPC 1973, under Article 100(b) EPC for insufficiency of disclosure and under Article 100(c) EPC for amendments that contained subject-matter extending beyond the content of the application as originally filed.
- III. The documents cited during the opposition and appeal proceedings included the following:
- (1) Am. J. Resp. Crit. Care Med., 1995, vol. 152, 32-37
 - (2) WO 94/08552
 - (3) Eur. J. Respir. Dis., 1983, 64 (suppl. 130), 17-24
 - (4) Allergy, 1990, 45, 382-385
 - (5) J. Aerosol Medicine, 1993, 6(2), 99-110
 - (6) WO 96/09814
 - (14) US-A-5 354 562
 - (15) US-A-5 354 934
 - (17) WO 95/24183
 - (31) Diabetic Medicine, 2004, 21, 763-768
- IV. The present appeal lies from an interlocutory decision of the opposition division, pronounced on 9 October 2006, to maintain the patent in amended form on the basis of auxiliary request 1, filed during oral

proceedings before the opposition division. The main request, which was also filed during the oral proceedings, was found to lack an inventive step.

V. The independent claims of the two requests read as follows:

(i) main request:

"1. Use of a dry powder drug for the manufacture of medicament for inhalation, wherein said inhalation comprises the steps of:

a) providing a dry powder drug composition having a drug particle size of from 1-7 microns and mass median aerodynamic diameter of the delivered aerosol of from 3 to 6 microns wherein the drug comprises a protein, polypeptide or hormone;

b) loading the dry powder drug composition into a dry powder inhaler which is generally flow rate independent, and with the inhaler having an inspiration flow resistance of 0.12 to 0.21 (cm H₂O)^{1/2} over the range of 15-60 L/min;

c) inhaling the drug composition from the inhaler with an inspiration flow rate of 15-60 L/min, resulting in a delivery efficiency measured by respirable fraction of at least 20%."

(ii) auxiliary request 1:

The sole independent claim 1 is identical to claim 1 of the main request, except that the passage "wherein the drug comprises a protein, polypeptide or hormone" was replaced by "wherein the drug comprises a protein or a polypeptide".

VI. Regarding the main request, the opposition division came to the conclusion that the change from a method of inhalation to a Swiss-type claim in claim 1 did not result in added subject-matter. Neither did the introduction of the feature "wherein the drug comprises a protein, polypeptide or hormone" in step a) which had a basis in claim 4 as well as in the last paragraph on page 5 of the application as filed. The feature "dry powder inhaler" was implicitly disclosed in claim 1 of the original application, as it was clear that the inhaler mentioned in said claim 1 had to be a dry powder inhaler since the drug to be delivered was in the form of a dry powder. The range of 15-60 L/min had its basis in claim 10 and on page 6, lines 7-8 of the original application. As a consequence, the requirements of Article 123(2) EPC were met.

In connection with Article 123(3) EPC, the opposition division reasoned that the replacement of the range 10-60 L/min in claim 1 as granted by the range 15-60 L/min in claim 1 of the main request resulted in an extension of the groups of inhalers defined in step b) since the requirement of having a flow resistance of 0.12 to 0.21 over a narrower range of inspiration flow rates was less stringent than having the same resistance over a broader range. However, in view of the fact that the range of 15-60 L/min was disclosed in claim 10 as granted, which referred back to claim 1, there was no extension of the protection conferred. In view of the fact that claim 1 was drafted in the Swiss-type format, it was not excluded from patentability pursuant to Article 52(4) EPC 1973. Being directed to the use of a substance for the preparation of a

pharmaceutical product, the subject-matter of claim 1 also met the requirements of Article 57 EPC.

As regards sufficiency of disclosure, the opposition division concluded that the information in paragraphs [0011] and [0012] of the contested patent ("Detailed Description") in combination with the reference to document (2) enabled the skilled person to carry out the invention without undue burden.

The subject-matter of claim 1 of the main request was novel, as none of documents (1) to (4) related to the use of proteins, polypeptides or hormones.

As regards inventive step, document (2) was defined as closest prior art. In view of the fact that the use as defined in claim 1 of the main request included both proteins and polypeptides on the one hand and hormones on the other hand and taking into consideration that no beneficial effects had been shown for the hormones, the problem to be solved in relation to the use of hormones was defined as the provision of a method for dry powder inhalation of hormones. Starting from document (2), the opposition division concluded that the selection of the specific parameters defined in claim 1 did not provide any particular effect on the efficiency of delivery as far as the use of hormones was concerned. Hence, the subject-matter as claimed in the main request lacked an inventive step.

As regards an inventive step of the subject-matter according to claim 1 of auxiliary request 1, in which the active agents to be used are limited to hormones and polypeptides, the opposition division, again

choosing document (2) as closest prior art, defined the problem to be solved as the provision of a method for dry powder inhalation of proteins and polypeptides which provided an efficient systemic delivery. Document (2) indicated that an adjustment of the flow parameters to the specific drug to be delivered was necessary for increasing the efficiency of systemic delivery but failed to provide instructions for the specific case of a protein. As a consequence, document (2) alone did not render obvious the subject-matter claimed in auxiliary request 1. Neither did the combination of document (2) with documents (15) or (1). Document (15) was not pertinent, firstly because it related to the Spinhaler, the inspiration flow resistance of which was well away from the range defined in present claim 1, and secondly, because it did not mention the inspiration flow rate. Document (1) was not pertinent, as it did not relate to dry powder delivery systems at all.

VII. All parties (appellant-proprietor, appellant-opponent 01, appellant-opponent 02 and appellant-opponent 03) lodged an appeal against that decision.

VIII. With the statement of the grounds of appeal dated 19 April 2007, the appellant-proprietor filed a main request and auxiliary requests 1 to 4. The sole independent claims read as follows:

(i) main request:

Claim 1 is identical to claim 1 of the main request filed at the oral proceedings of 9 October 2006.

(ii) auxiliary request 1:

Claim 1 is identical to claim 1 of the main request except that "wherein the drug comprises a protein, polypeptide or hormone" in step a) was replaced by "wherein the drug comprises a systemic, or a topical drug for treating asthma".

(iii) auxiliary request 2:

Claim 1 is identical to claim 1 of the main request except that the words "Use of a dry powder drug for the manufacture of medicament for inhalation" was replaced by "Use of a dry powder drug for the manufacture of medicament for systemic delivery by inhalation".

(iv) auxiliary request 3:

"1. Use of a dry powder drug for the manufacture of medicament for systemic delivery by inhalation, wherein said inhalation comprises the steps of:

- a) providing a dry powder drug composition having a drug particle size of from 1-7 microns and mass median aerodynamic diameter of the delivered aerosol of from 3 to 6 microns wherein the drug comprises a protein, polypeptide or hormone;
- b) loading the dry powder drug composition into a dry powder inhaler which is generally flow rate independent, and with the inhaler having an inspiration flow resistance of 0.12 to 0.21 (cm H₂O)^{1/2} over the range of 15-60 L/min;
- c) inhaling the drug composition from the inhaler with an inspiration flow rate of 15-60 L/min, resulting in a delivery efficiency measured by respirable fraction of

greater than 30%, wherein the respirable fraction is the fraction of particles penetrating the impactor inlet with a particle size less than 5.8 microns."

(v) auxiliary request 4:

Claim 1 is identical to claim 1 of auxiliary request 1 filed at the oral proceedings of 9 October 2006.

IX. With a letter dated 26 September 2007, the appellant-proprietor filed auxiliary requests 5 to 10. The sole independent claims read as follows:

(vi) auxiliary request 5:

Claim 1 is identical to claim 1 of auxiliary request 4 except that "Use of a dry powder drug for the manufacture of medicament for inhalation" was replaced by "Use of a dry powder drug for the manufacture of medicament for systemic delivery by inhalation".

(vii) auxiliary request 6:

Claim 1 is identical to claim 1 of auxiliary request 4 except that "dry powder inhaler" in step b) was replaced by "inhaler".

(viii) auxiliary request 7:

"1. Use of a dry powder drug for the manufacture of medicament for inhalation, wherein said inhalation comprises the steps of:

a) providing a dry powder drug composition which includes an inert carrier having a drug particle size

of from 1-7 microns and mass median aerodynamic diameter of the delivered aerosol of from 3 to 6 microns wherein the drug comprises a protein or polypeptide;

b) loading the dry powder drug composition into an inhaler which is generally flow rate independent, and with the inhaler having an inspiration flow resistance of 0.12 to 0.21 (cm H₂O)^{1/2} over the range of 10-60 L/min;

c) inhaling the drug composition from the inhaler with an inspiration flow rate of 15-60 L/min, resulting in a delivery efficiency measured by respirable fraction of at least 20%."

(ix) auxiliary request 8:

Claim 1 is identical to claim 1 of the main request except that "Use of a dry powder drug for the manufacture of medicament for inhalation" was replaced by "Use of a dry powder drug for the manufacture of medicament for treatment of a condition other than a lung condition by inhalation".

(x) auxiliary request 9:

Claim 1 is identical to claim 1 of the main request except that "wherein the drug comprises a protein, polypeptide or hormone" in step a) was replaced by "wherein the drug comprises a polypeptide".

(xi) auxiliary request 10:

Claim 1 is identical to claim 1 of the main request except that "Use of a dry powder drug for the

manufacture of medicament for inhalation" was replaced by "Use of a dry powder drug for the manufacture of medicament for treating lung conditions by inhalation" and that "wherein the drug comprises a protein, polypeptide or hormone" in step a) was replaced by "wherein the drug comprises a topical drug for treating asthma".

X. With a letter dated 7 January 2011, the appellant-proprietor declared that he would not be attending the oral proceedings scheduled for 7 February 2011.

XI. Oral proceedings were held before the board on 7 February 2011.

XII. In connection with inventive step, the appellant-proprietor's arguments can be summarised as follows:

The identification of document (2) as closest prior art required a knowledge of the claimed invention which could only be found in the contested patent and therefore amounted to the use of hindsight. Document (2) made reference neither to peptides, polypeptides or hormones or to the systemic delivery of these compounds, nor to the inspiration flow rate resistance, inspiration flow rate, MMAD or particle size and was therefore not pertinent. If document (2) was taken as closest prior art, the problem to be solved could be defined as the provision of an efficient systemic delivery of proteins, polypeptides and hormones. The skilled person faced with this problem got no motivation to choose the device parameter, powder parameters and inhalation parameters as claimed. In view of document (31), which showed that insulin, which

was a hormone as well as a protein, could also be efficiently delivered by the system of the claimed invention, an inventive step should be acknowledged not only for peptides or polypeptides, but also for the hormones. Document (1) was not relevant to the problem addressed by the invention. There was no indication that the conclusions of document (1) could be generalised beyond the teaching that Teflon aerosols were delivered to certain asthmatics using a Beckman Atomizer. Furthermore, the attempt of appellant-opponents 02 and 03 to combine the teachings of documents (1) and (2) with the teaching of a further document such as (14), (15) or (17) was not permissible.

XIII. In connection with inventive step, the relevant arguments of the appellant-opponents can be summarised as follows:

Appellant-opponent 03 emphasised at the oral proceedings before the board that inventive step was only an issue if the claims were regarded as correctly construed "Swiss-type claims". If, however, said claims were considered to relate to a method for preparing a medicament, then there was lack of novelty. As regards inventive step, document (2) was a suitable starting point. As for the fact that document (2) neither specifically mentioned polypeptides or proteins as drugs nor the specific combination of parameters defining particle size, flow resistance and inspiration flow rate, the appellant-opponent 03 argued that there was no evidence for any particular effect resulting from this accumulation of parameters. It was not at all evident that these parameters, which were commonly used

in the prior art as could be deduced e.g. from documents (5) or (6), provided an unexpected effect compared to other parameters that might have been chosen instead. A skilled person must be able to choose the right parameters in order to correctly operate an inhaler as disclosed in document (2) without applying inventive skill. As a consequence, the claimed subject-matter lacked an inventive step.

XIV. The appellant-proprietor requested in writing that the decision under appeal be set aside and the patent be maintained on the basis of the main request or, in the alternative, on the basis of one of auxiliary requests 1 to 4 filed with the statement of the grounds of appeal dated 19 April 2007, or on the basis of one of auxiliary requests 5 to 10 filed with letter dated 26 September 2007.

The appellant-opponents requested in writing and in case of appellant-opponent 03 also at the oral proceedings that the decision under appeal be set aside and that the European patent No. 0 896 525 be revoked.

Reasons for the Decision

1. The appeals are admissible.
2. Inventive step:
 - 2.1 Main request:

The present invention concerns the use of a dry powder drug for the manufacture of a medicament for inhalation

by means of a dry powder inhaler (see paragraph [0005] and claim 1 of the patent specification).

Document (2), which constitutes the closest prior art, relates to a dry powder inhaler which is substantially flow rate independent and which provides significant resistance to air flow (= inspiration flow resistance) (see page 1, lines 2-3; page 3, lines 10-11 and page 7, lines 16-22). The dry powder inhaler according to document (2) is not designed for a specific drug, but allows the adjustment of flow parameters to the specific drug to be delivered (see page 18, lines 13-15).

In the light of this prior art, the problem to be solved is the provision of a method for delivering a medicament for a dry powder inhaler which is substantially flow rate independent and which provides significant inspiration flow resistance.

As a solution to this problem, the contested patent proposes the use defined in present claim 1, wherein a protein, a polypeptide or a hormone comprising a certain particle size and a certain aerodynamic diameter was chosen together with a specific inspiration flow resistance and a specific inspiration flow rate.

In the light of the teaching according to paragraph [0005] of the contested patent, the board is satisfied that the problem defined above was plausibly solved.

As for the appellant-proprietor's objection that the selection of document (2) as closest prior art was the result of hindsight, the board notes that the selection of the closest prior art requires the skilled person's knowledge of the whole state of the art at the effective filing date of the original application. The selection of document (2) can therefore not be based on hindsight. Hindsight, however, is not permissible in the later stage of the problem-solution approach, i.e. in the process of evaluating whether the solution to the problem as defined in the light of the closest prior art, is obvious to the skilled person. As a consequence, document (2) was correctly chosen as closest prior art.

For defining the technical problem vis-à-vis document (2), and in particular for determining whether or not the subject-matter as defined in present claim 1 constitutes an improved administration, alleged effects not having their origin in the distinguishing feature(s) of the invention cannot be taken into consideration.

In the present case, there is no evidence that the high delivery efficiency is due to the choice of the drug and/or of the parameters mentioned above. On the contrary, the teaching found in the original application clearly indicates that the high delivery efficiency is the result of the specific inhaler, i.e. the inhaler according to document (2) (see the original application page 2, line 26 - page 3, lines 2; page 4, lines 23-26 and page 5, lines 3-5).

As regards step a) of claim 1, it is noted that the use of proteins, polypeptides or hormones is common practice in the prior art. Thus, document (6), which concerns the administration of active agents to the pulmonary airways, mentions proteinaceous material such as insulin, parathyroid hormone, calcitonin or similar bioactive peptide, albuterol, salicylate, naproxen, augmentin or a cytotoxic agent as active agents for such an administration (see page 13, lines 6-9). The particles to be administered preferably have a mass median diameter of 1 to 10 μm (see page 5, lines 25-30). Moreover, document (6) states that for accessing the lowest regions of the pulmonary airways, particles should have an aerodynamic diameter of $<5 \mu\text{m}$. Particles above this size will be caught by impaction in the upper airways (see page 1, lines 27-34).

As for step b) of claim 1, it is again emphasised that the inhaler according to document (2) provides for a inspiration flow resistance in order to reduce impaction of the particles against the rear of the user's throat (see page 7, lines 16-22). Document (2) does not disclose the specific range of 0.12 to 0.21 (cm H₂O)^½ but such values are commonly found in connection with conventional inhalers such as Turbohaler or Inhalator (see table 1 on page 102 of document (5)).

Lastly, the inspiration flow rate of 15-60 L/min is also common in the prior art and adapted to the patients' needs. Thus document (5) describes an assay in which the maximum and the comfortable flow rates were determined. The persons involved in this test defined 60 L/min, i.e. the upper limit of the claimed

range, as a comfortable flow rate (see first complete paragraph on page 103).

To summarise: in order to solve the problem defined above, the patentee resorted to features which are commonly used in the prior art and which do not contribute to an improved delivery efficiency. Such a compilation of known features for operating a known inhaler does not involve an inventive step. It is again emphasised that the delivery efficiency measured by respirable fraction of at least 20% defined in step c) of claim 1 is the result of the choice of the inhaler according to document (2) so that the delivery efficiency cannot establish an inventive step. As a consequence, the requirements of Article 56 EPC are not met.

2.2 Auxiliary request 1:

Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the active agent is now a systemic, or a topical drug for treating asthma. In view of the fact that the list of drugs in document (6) includes active agents such as albuterol (see page 13, line 8), which is used for treating asthma, the reasoning of point 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 1. The requirements of Article 56 EPC are therefore not met.

2.3 Auxiliary request 2:

Claim 1 of auxiliary request 2 differs from claim 1 of the main request in that the claimed use now concerns the systemic delivery of the drug by inhalation. In

view of the fact that administration of a drug via inhalation is a systemic application, the reasoning of point 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 2. The requirements of Article 56 EPC are therefore not met.

2.4 Auxiliary request 3:

Claim 1 of auxiliary request 3 differs from claim 1 of auxiliary request 2 in that delivery efficiency is now greater than 30%. In view of the fact that delivery efficiency is the consequence of the selected inhaler, i.e. the inhaler disclosed in document (2), the reasoning of point 2.3 in combination with point 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 3. The requirements of Article 56 EPC are therefore not met.

2.5 Auxiliary request 4:

Claim 1 of auxiliary request 4 differs from claim 1 of the main request in that the hormones were deleted from the list of drugs. In view of the fact that the list of drugs in document (6) includes insulin or other bioactive peptides (see page 13, lines 6-9), the reasoning of point 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 4. The requirements of Article 56 EPC are therefore not met.

2.6 Auxiliary request 5:

Claim 1 of auxiliary request 5 differs from claim 1 of auxiliary request 2 in that the hormones were deleted from the list of drugs. In view of the fact that the

list of drugs in document (6) includes insulin or other bioactive peptides (see page 13, lines 6-9), the reasoning of points 2.1 and 2.3 above applies *mutatis mutandis* to claim 1 of auxiliary request 5. The requirements of Article 56 EPC are therefore not met.

2.7 Auxiliary request 6:

Claim 1 of auxiliary request 6 differs from claim 1 of auxiliary request 4 in that the "dry powder inhaler" in step b) was generalised to "inhaler". As the subject-matter of claim 1 of auxiliary request 6 still includes dry powder inhalers, the reasoning of point 2.5 in combination with point 2.1 above also applies to claim 1 of auxiliary request 6. The requirements of Article 56 EPC are therefore not met.

2.8 Auxiliary request 7:

Claim 1 of auxiliary request 7 differs from claim 1 of auxiliary request 6 in that the powder drug composition of step a) additionally comprises an inert carrier and in that the range for the inspiration flow resistance of 0.12 to 0.21 (cm H₂O)^½ was increased from 15-60 L/min to 10-60 L/min. In view of the fact that inert carriers are common in the field of powders for inhalation and are disclosed e.g. in document (6) in combination with a particle size of 1 to 10 µm (see page 5, lines 25-30), and taking into consideration that no technical effect can be associated to said enlarged range, the reasoning of point 2.7 in combination with points 2.5 and 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 7. The requirements of Article 56 EPC are therefore not met.

2.9 Auxiliary request 8:

Claim 1 of auxiliary request 8 differs from claim 1 of the main request in that the medicament is now to be used for the treatment of a condition other than a lung condition. In view of the fact that the list of drugs in document (6) includes insulin, which is used for the treatment of diabetes (see page 13, line 7), the reasoning of point 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 8. The requirements of Article 56 EPC are therefore not met.

2.10 Auxiliary request 9:

Claim 1 of auxiliary request 9 differs from claim 1 of the main request in that the list of drugs in step a) is now reduced to polypeptides. In view of the fact that the list of drugs in document (6) includes insulin or other bioactive peptides (see page 13, lines 6-9), the reasoning of point 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 9. The requirements of Article 56 EPC are therefore not met.

2.11 Auxiliary request 10:

Claim 1 of auxiliary request 10 differs from claim 1 of the main request in that the medicament is used for treating lung conditions and in that the active agent is now a topical drug for treating asthma. In view of the fact that the list of drugs in document (6) includes active agents such as albuterol (see page 13, line 8), which is used for treating asthma, and taking into consideration that the treatment of lung

conditions includes the treatment of asthma, the reasoning of point 2.1 above applies *mutatis mutandis* to claim 1 of auxiliary request 1. The requirements of Article 56 EPC are therefore not met.

3. In view of this finding, an evaluation of the further objections raised by the appellant-opponents is not necessary.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:

N. Maslin

U. Oswald