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Datasheet for the decision of 2 November 2022

Case Number: T 0784/20 - 3.3.07

Application Number: 10185643.3

Publication Number: 2283818

IPC: A61K9/14, A61K9/72, A61K9/00

Language of the proceedings: EN

Title of invention:
Method of making particles for use in a pharmaceutical composition

Patent Proprietor:
Vectura Limited

Opponent:
Glaxo Group Limited

Headword:
Composite particles/VECTURA

Relevant legal provisions:
EPC Art. 56
RPBA 2020 Art. 11

Keyword:

Inventive step - obvious alternative
Remittal - (no)

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Case Number: T 0784/20 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 2 November 2022

Appellant: (Patent Proprietor)	Vectura Limited 1 Prospect West Chippenham, Wiltshire SN14 6FH (GB)
Representative:	CMS Cameron McKenna Nabarro Olswang LLP Cannon Place 78 Cannon Street London EC4N 6AF (GB)
Appellant: (Opponent)	Glaxo Group Limited 980 Great West Road Brentford Middlesex TW8 9GS (GB)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 7 February 2020 concerning maintenance of the European Patent No. 2283818 in amended form.**

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	Y. Podbielski

Summary of Facts and Submissions

I. European patent 2 283 818 ("the patent") was granted on the basis of fifteen claims.

Independent claim 1 as granted related to:

"A method for making composite active particles for use in a pharmaceutical composition for pulmonary administration, the method comprising a milling step in which particles of active material are milled in the presence of particles of an additive material which is suitable for the promotion of the dispersal of the composite active particles upon actuation of an inhaler, wherein the additive material is magnesium stearate."

Independent claim 8 as granted related to composite active particles for use in a pharmaceutical composition as made by such method. Independent claim 12 as granted related to a pharmaceutical composition comprising composite active particles as made by such method.

II. The patent was opposed on the grounds that its subject-matter lacked novelty and lacked inventive step, that the claimed invention was not sufficiently disclosed and that the patent comprised subject-matter extending beyond the content of the (earlier) application as filed

The patent proprietor and the opponent filed appeals against the interlocutory decision of the opposition division that the patent as amended in accordance with auxiliary request 1 as filed during the oral

proceedings held on 25 September 2019 met the requirements of the EPC.

The decision was based on the main request of 25 July 2019 (originally filed as auxiliary request 1) and the mentioned auxiliary request 1.

In its decision the opposition division cited *inter alia* the following documents:

D1: WO 00/27363
D7: International Journal of Pharmaceutics 173 (1998) 243-251
D15: Handbook of Pharmaceutical Excipients (2nd edition, 1994) p. 280-282
D16: Handbook of Pharmaceutical Excipients (3rd edition, 2000) p. 305-308
D18: WO 96/23485
D30: Extract from thesis submitted to King's College, University of London, by Nuha Kassem in 1990.

The opposition division arrived at the following conclusions:

(a) The claims of the main request corresponded to the claims as granted with deletion of two dependent claims.

The main request did not comprise subject-matter extending beyond the original disclosure.

The subject-matter of claim 1 of the main request lacked novelty in view of document D18, which described a dry powder for pulmonary administration prepared from milling a ternary mixture including particulate magnesium stearate.

(b) The claims of auxiliary request 1 additionally included the originally preferred feature that the mass median aerodynamic diameter (MMAD) of the composite active particles is not more than 10 µm.

Auxiliary request 1 complied with the requirements of Articles 83 and 123(2) EPC.

The defined subject-matter was entitled to the priority of 30 November 2000 and was new over the prior art, including document D18, which did not disclose the MMAD defined in the claims of auxiliary request 1.

Document D7 represented the closest prior art. The claimed subject-matter differed from the teaching in document D7 in the use of magnesium stearate as the additive material instead of Aerosil® 200. The problem to be solved was the provision of an alternative method for making particles with improved suitability for pulmonary administration. From document D30 the additives Aerosil® 200 and magnesium stearate were known to behave differently. No prior art suggested the replacement of the hydrophilic Aerosil® 200 by the hydrophobic magnesium stearate as solution. The subject-matter of auxiliary request 1 therefore involved an inventive step.

III. With the statement of grounds of appeal the appellant-patent proprietor filed a main request and auxiliary requests 1-6. The appellant-proprietor additionally filed auxiliary requests 7-9 with the reply to the appeal by the opponent.

The main request corresponds to the main request on which the decision under appeal is based and thus relates to the claims as granted from which two dependent claims as granted were deleted.

The claims of auxiliary request 1 correspond to the claims of auxiliary request 1 on which the decision under appeal was based, in which claim 1 additionally defines with respect to claim 1 of the main request that the MMAD of the composite active particles is not more than 10 µm.

The claims of auxiliary request 2 differ from the claims of auxiliary request 1 in the specification of the defined MMAD as determined using a multi stage liquid impinger.

Auxiliary request 3 is limited to claim 1 of auxiliary request 2 and the independent product claims.

The claims of auxiliary request 4 differ from the claims of auxiliary request 3 in the additional definition that the additive material is in the form of a discontinuous coating.

The claims of auxiliary request 5 differ from the claims of auxiliary request 4 in that the defined MMAD concerns the composite active particles after the milling step.

Auxiliary request 6 is limited to claim 1 of auxiliary request 5.

Auxiliary requests 7-9 correspond respectively to the main request and auxiliary requests 1 and 2 in which

the dependent product claims defining a discontinuous coating are deleted.

IV. With the statement of grounds of appeal the appellant-opponent maintained *inter alia* that the subject-matter of the first auxiliary request lacked an inventive step in view of document D1 as starting point in the prior art. The appellant-opponent further argued that this objection also applied with respect to subject-matter additionally characterized by the feature of the additive material forming a discontinuous coating or the feature that the MMAD is determined by a particular method.

V. The Board invited the parties to attend oral proceedings on 14 October 2022.

In its communication pursuant to Article 15(1) RPBA the Board expressed *inter alia* the preliminary opinion that document D1 represented a suitable starting point for the assessment of an inventive step and that no special reason for remittal under Article 11 RPBA 2020 was recognized in the mere fact that the decision under appeal did not address the issue of document D1 as a suitable starting point in the prior art.

VI. With the letter of 22 September 2022 the appellant-patent proprietor withdrew its request for oral proceedings and announced not to attend the oral proceedings scheduled for 14 October 2022.

VII. The oral proceedings were cancelled with the Boards communication of 28 September 2022.

VIII. The arguments of the appellant-patent proprietor relevant to the present decision can be summarized as follows:

The issue of inventive step, in particular the closest prior art with respect to the main request, had not been fully examined and decided on by the first instance. The appellant-opponent proposed a multitude of starting points, including a new starting point, namely document D1, which had not been addressed in the decision under appeal. This constituted a special reason for remittal.

Document D7 represented the closest prior art describing the use of Aerosil 200 as surface modifier instead of magnesium stearate as defined for the invention as claimed in accordance with the main request and auxiliary requests 1-9. The problem to be solved concerned the provision of an improved method for making particles suitable for inhalation. No prior art suggested the use of milling the active material with hydrophobic magnesium stearate instead of the hydrophilic Aerosol 200. Document D1, which was presented as an alternative starting point, listed with reference to document D15 a plurality of potential surface modifiers, but failed to disclose or suggest magnesium stearate as a suitable additive. Document D15, which was taken from a handbook on pharmaceutical excipients, as well as document D16, which represented the corresponding section of the subsequent edition of this handbook, actually explicitly warned against the harmful inhalation of magnesium stearate.

IX. The arguments of the appellant-opponent relevant to the present decision can be summarized as follows:

Document D1 described surface modified drug particles for delivery to the respiratory tract and thus concerned the same problem as addressed in the patent. The subject-matter claimed in accordance with the main request and the first auxiliary request differed from the teaching of document D1 in the definition of magnesium stearate as the surface modifier. As no comparative data demonstrated any advantage over the surface modifiers described in document D1, the problem to be solved concerned the provision of an alternative method for preparing particles for pulmonary administration. Document D1 already described surfactants in general as suitable surface modifiers and mentioned calcium stearate as an example. At the same time magnesium stearate was, as evidenced by documents D15 and D16, a well known alternative surfactant for pharmaceutical application. The claimed subject-matter therefore lacked an inventive step.

No data indicated any technical significance associated with the feature of the additive material forming a discontinuous coating. Moreover, the indication that the MMAD was determined by a particular method did not affect the scope of the claims. Accordingly, the same objection of lack of inventive step also applied with respect to subject-matter additionally characterized by these features.

X. The appellant-patent proprietor requested that the decision under appeal be set aside and that the case be remitted to the opposition division for consideration of the main request under Article 56 EPC.

As an auxiliary measure the appellant-patent proprietor requested that the patent be maintained on the basis of one of auxiliary requests 1-6 as filed with the

statement of grounds of appeal or auxiliary requests 7-9 as filed with the reply to the appeal by the opponent.

XI. The appellant-opponent requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

Reasons for the Decision

1. Request for remittal

The Board observes that whilst the decision under appeal (see page 10, section 9.4) identifies document D7 as closest prior art with respect to the subject-matter of claim 1 of auxiliary request 1, document D1 had been relied upon as a suitable starting point for the assessment of inventive step by the appellant-opponent in its notice of opposition (see pages 18-19, section 7.3). The objection of lack of inventive step based on document D1 as an alternative suitable starting point by the appellant-opponent does therefore not represent a new objection raised for the first time upon appeal.

No substantive arguments were submitted by the appellant-patent proprietor in response to the preliminary opinion expressed by the Board in its communication pursuant to Article 15(1) RPBA (see page 13, section 5.1) that no special reason for remittal under Article 11 RPBA 2020 was to be recognized in the mere fact that the decision under appeal did not address the issue of document D1 as suitable starting point in the prior art.

Accordingly, the Board rejects the appellant-patent proprietor's request for remittal of the case to the opposition division for consideration of the main request under Article 56 EPC.

2. Main request, inventive step

2.1 Starting point in the prior art

Each of documents D1 and D7 describe the provision of surface modified drug particles. Both documents concern the same purpose and effect as the patent, namely the provision of surface modified drug particles with improved inhalation properties.

Document D1 describes surfactants as preferred surface modifiers (see D1 page 26 lines 13-14). The document further mentions calcium stearate in a list of surface modifiers (see page 26 line 18) and presents actual preparative examples involving milling using polyvinylpovidone (PVP) as surface modifier (see in particular D1 page 32 example 3). Document D7 describes the use of Aerosil 200 as surface modifier (see D7 page 244 column 2 lines 16-26). The subject-matter of claim 1 of the main request differs from the teaching of document D1 as well as document D7 in the choice of magnesium stearate as the surface modifier.

In its communication pursuant to Article 15(1) RPBA (see pages 14-15, section 5.2.4) the Board expressed its preliminary opinion that for these reasons document D1 did not present a less relevant starting point in the prior art with respect to the claimed invention than document D7, which was relied upon by the appellant-patent proprietor as closest prior art.

No substantive arguments were submitted by the appellant-patent proprietor in response to this preliminary opinion. Accordingly, the Board confirms that document D1 represents a suitable starting point for the assessment of inventive step with respect to the claimed subject-matter.

2.2 Problem to be solved

The appellant-proprietor identified the provision of an improved method for making particles suitable for inhalation as the problem to be solved. However, as observed in the Board's communication pursuant to Article 15(1) RPBA (see page 15, section 5.3) no particular advantage of the use of magnesium stearate with respect to the prior art of document D1 had been relied upon by the appellant-patent proprietor. This observation has not been contested by the appellant-patent proprietor.

The Board therefore confirms its preliminary opinion that the problem to be solved underlying the subject-matter defined in claim 1 of the main request is the provision of an alternative method of preparing surface modified particles for pulmonary administration.

2.3 Assessment of the solution

Document D1 describes surfactants in general as suitable surface modifiers and mentions calcium stearate as an example (see D1, page 26, line 18).

The document refers in this context specifically to the handbook on pharmaceutical excipients from which document D15 originates (see D1, page 27, lines 23-26).

Documents D15 and D16, which as excerpts from handbooks represent common knowledge, mention in the context of pharmaceutical excipients calcium stearate as a substance related to magnesium stearate (see D15, page 281, right column, under "18. Related Substances"; see D16, page 306, right column, under "18. Related Substances").

The Board considers that in the absence of convincing indications to the contrary the skilled person had therefore good reason to expect that magnesium stearate would be suitable as alternative to the surface modifier calcium stearate mentioned in document D1.

The appellant-patent proprietor referred in this context to the warnings mentioned in documents D15 and D16 regarding harmful inhalation of magnesium stearate (see D15, page 281, right column, under "14. Safety" and "15. Handling Precautions"; see D16, page 306, right column, under "15. Handling Precautions"). The Board observes, however, that these warnings evidently concern precautions aimed at avoiding harm from excessive inhalation of magnesium dust when handling the bulk substance. As pointed out by the appellant-opponent and not contested by the appellant-patent proprietor, the claimed subject-matter relates to pharmaceutical compositions for pulmonary administration in which only limited amounts of magnesium stearate are inhaled. The mentioned handling precautions against excessive inhalation are therefore not considered to affect the skilled person's expectation regarding the suitability of magnesium stearate for use as an alternative to the surface modifiers described in document D1.

Accordingly, the Board concludes that the subject-matter of claim 1 of the main request does not involve an inventive step.

3. Auxiliary requests 1-9, inventive step

As pointed out by the appellant-opponent (grounds of appeal, page 18, point 7.16), document D1 describes in example 3 a powder with a resultant MMAD of 1.67 µm (see D1, page 33, line 6). The feature that the MMAD of the composite active particles is not more than 10 µm, be it after milling, as required according to auxiliary requests 1-6 and 8-9 does therefore not represent a differentiating feature with respect to document D1.

Moreover, as argued by the appellant-opponent and not contested by the appellant-patent proprietor, the definition of this MMAD as determined using a multi stage liquid impinger in accordance with auxiliary requests 2-6 and 9 does not further distinguish the claimed subject-matter from the teaching in document D1.

As further pointed out by the appellant-opponent and not contested by the appellant-patent proprietor, no data on file indicate any technical significance supportive of an inventive step associated with the feature of the additive material forming a discontinuous coating as defined according to auxiliary requests 4-6.

Furthermore, claim 1 of auxiliary request 7 is identical to claim 1 of the main request.

The appellant-patent proprietor did in fact not argue that any of the additional features required according

to auxiliary request 1-9 supported an inventive step and merely referred with respect to the issue of inventive step regarding the auxiliary requests to its argumentation with respect to the main request.

Accordingly, the Board concludes that auxiliary requests 1-9 do not comply with the requirement of inventive step for the same reason as presented for the main request.

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:

S. Sánchez Chiquero A. Usuelli

Decision electronically authenticated