

**Internal distribution code:**

- (A) [ - ] Publication in OJ
- (B) [ - ] To Chairmen and Members
- (C) [ - ] To Chairmen
- (D) [ X ] No distribution

**Datasheet for the decision  
of 21 February 2020**

**Case Number:** T 2720/17 - 3.3.07

**Application Number:** 11190637.6

**Publication Number:** 2422766

**IPC:** A61K9/00, A61K47/12, A61K31/40

**Language of the proceedings:** EN

**Title of invention:**  
Dry powder compositions of glycopyrrolate and magnesium stearate

**Patent Proprietor:**  
Vectura Limited

**Opponents:**  
Teva UK Limited  
FRKelly

**Headword:**  
Dry powder formulation of glycopyrrolate / VECTURA

**Relevant legal provisions:**  
EPC Art. 56  
RPBA 2020 Art. 12(3)

**Keyword:**

Inventive step - (no)



**Beschwerdekammern**  
**Boards of Appeal**  
**Chambres de recours**

Boards of Appeal of the  
European Patent Office  
Richard-Reitzner-Allee 8  
85540 Haar  
GERMANY  
Tel. +49 (0)89 2399-0  
Fax +49 (0)89 2399-4465

Case Number: T 2720/17 - 3.3.07

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.07**  
**of 21 February 2020**

**Appellant:** Vectura Limited  
(Patent Proprietor) 1 Prospect West  
Chippenham, Wiltshire SN14 6FH (GB)

**Representative:** CMS Cameron McKenna Nabarro  
Olswang LLP  
Cannon Place  
78 Cannon Street  
London EC4N 6AF (GB)

**Respondent:** Teva UK Limited  
(Opponent 1) Ridings Point  
Whistler Drive  
Castleford WF10 5HX (GB)

**Representative:** Elkington and Fife LLP  
Prospect House  
8 Pembroke Road  
Sevenoaks, Kent TN13 1XR (GB)

**Respondent:** FRKelly  
(Opponent 2) 27 Clyde Road  
Ballsbridge  
Dublin 4 (IE)

**Representative:** FRKelly  
27 Clyde Road  
Dublin D04 F838 (IE)

**Decision under appeal:** **Decision of the Opposition Division of the  
European Patent Office posted on 26 October 2017  
revoking European patent No. 2422766 pursuant to  
Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairman**           A. Usuelli  
**Members:**         E. Duval  
                      P. Schmitz

## **Summary of Facts and Submissions**

- I. European patent 2 422 766 (hereinafter "the patent") was granted on the basis of 11 claims. Claim 1 of the patent as granted read as follows:

"A dry powder formulation suitable for inhalation comprising glycopyrrolate and magnesium stearate, wherein the glycopyrrolate is micronised and then undergoes a conditioning step, which step includes exposure to humid conditions of 50-90% RH at temperatures between 10 to 50°C for at least 48 hours."

- II. Two oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application and the earlier application as filed.

- III. The opposition division took the decision to revoke the patent. The decision was based on the patent as granted as main request and on auxiliary requests 1-3 filed by letter dated 12 September 2016.

Claim 1 of Auxiliary request 1 differed from claim 1 of the main request by the following additional feature:

"and wherein the powder is agitated or turned during conditioning to ensure that all of the particles are equally exposed to the humid atmosphere."

Claim 1 of Auxiliary request 2 differed from claim 1 of the main request by the following additional feature:

"and wherein the magnesium stearate is predominantly present on the surface of the glycopyrrolate particles."

Claim 1 of Auxiliary request 3 differed from claim 1 of the main request by the following additional feature:

"wherein the formulation is stored in a hydroxypropyl methylcellulose capsule which has a moisture content of less than 10%, and wherein the hydroxypropyl methylcellulose capsules are stored in an additional layer of foil packaging."

IV. The following documents were among those cited in the decision under appeal:

D7: WO 02/43701

D8: WO 95/05805

D14: Experimental report of Vectura dated 6 March 2015

D15: Declaration of M.M.J. Green dated 6 March 2015

D16: Declaration of Associate Professor D. Morton, undated

V. According to the decision under appeal, none of the requests fulfilled the criteria of inventive step:

(a) With respect to the main request, D7 represented the closest prior art. The claimed dry powder formulation differed from those of D7 in that it was obtained by a method of preparation including a post micronisation conditioning step which included exposure of the micronised glycopyrrolate to humid conditions of 50-90%RH at temperature between 10°C and 50°C for at least 48 hours. An improved stability of the resulting, conditioned micronised glycopyrrolate was not shown. The problem was the

provision of an alternative stable dry powder formulation suitable for inhalation comprising micronised glycopyrrolate and magnesium stearate. The claimed solution was obvious in light of D8.

(b) Likewise, the subject-matter of each of the auxiliary requests 1-3 did not involve an inventive step in light of D7 and D8.

VI. The patent proprietor (appellant) lodged an appeal against the decision of the opposition division. In the statement setting out the grounds of appeal, the appellant contested the opposition division's finding of lack of inventive step and defended its case on the basis of the patent as granted as main request and on the basis of the auxiliary requests 1-3 filed during the proceedings before the opposition division.

VII. With their replies to the appeal of the patent proprietor, the opponents (respondents) expressed *inter alia* the view that none of the requests fulfilled the requirements of Article 56 EPC.

VIII. The Board issued summons to oral proceedings. In a communication pursuant to Article 15(1) RPBA, the Board expressed the preliminary opinion that none of the requests fulfilled the criteria of inventive step.

By letter dated 27 January 2020, the appellant withdrew its request for oral proceedings.

The Board cancelled the oral proceedings.

IX. The appellant's arguments, as far as relevant for the present decision, may be summarised as follows:

Regarding inventive step for the main request, the closest prior art was D7, because it addressed the same problem as the patent, which was to improve the respirable fraction of inhalable drug particles. Example 5 of D7 described composite small particles suitable for inhalation, made by mechanofusing pre-micronized glycopyrrolate particles in the presence of magnesium stearate. The method of D7 resulted in fully coated, completely stable particles.

D7 did not disclose a post-micronisation conditioning step in which the glycopyrrolate was exposed to defined humidity and temperature conditions for at least 48 hours. The technical effect resulting from this conditioning step was the production of a completely stable glycopyrrolate particle, such that small particle size and desirable inhalable properties were obtained upon aerosolisation from a dry powder inhaler. The problem was the provision of an alternative formulation of stabilised glycopyrrolate and magnesium stearate suitable for inhalation.

D7 already solved the problem of providing stable glycopyrrolate formulations using a coating process which made the active less cohesive after milling. Hence D7 taught away from the use of a post conditioning process, because it already solved the problem. Furthermore, the skilled person would not have combined the teaching of D7 with the conditioning step shown in D8 because glycopyrrolate was highly hygroscopic and was not specifically listed in D8, and because the skilled person would not have subjected the glycopyrrolate to an unnecessary extra processing step when there was no expectation of a benefit in doing so. Moreover, the skilled person would not consider micronising the glycopyrrolate, then conditioning, then



coating the glycopyrrolate as taught in D7, because the coating would reintroduce amorphous material, thereby reintroducing the problem.

The subject-matter of the main request thus involved an inventive step.

The subject-matter of auxiliary requests 1-3 met the requirements of inventive step for all the reasons set out in respect to the main request.

- X. The respondents' arguments, as far as relevant for the present decision, may be summarised as follows:

The closest prior art D7 related to dry powder formulation suitable for inhalation. It recognised the need to provide and maintain active materials having a size suitable for inhalation. D7 also mentioned that a milling process will tend to generate amorphous material on the surface of the milled particles thereby leading to agglomeration. According to D7, particles of the active material were milled in the presence of an additive material, thus resulting in a partial or complete coating. In example 5, the active agent was glycopyrrolate and the additive material magnesium stearate.

The distinguishing feature was not the conditioning step *per se*, since claim 1 of the main request was a product claim and not a process claim.

No data showed any advantage for the distinguishing feature. The objective technical problem was the provision of an alternative formulation to that of D7.

D8 provided a clear pointer to conditioning the active ingredient, directly after micronisation, under humid conditions as in the present invention in order to reduce the amorphous content and thereby improve stability. The skilled person was always concerned with continuous technical development and would have considered modifying the teaching of D7, even if the composition of D7 were already stable.

Accordingly, the subject-matter of the main request lacked an inventive step.

Auxiliary requests 1-3 had been filed during the opposition proceedings. At points 2-4 of the decision under appeal, the opposition division had set out the reasoning as to why these auxiliary requests were not allowable. The appellant had not addressed these reasons and had not provided any argumentation why the additional features over the main request could confer an inventive step. Therefore, auxiliary requests 1-3 similarly lacked an inventive step.

XI. The appellant requests that the decision under appeal be set aside and that the patent be maintained as granted, or, in the alternative, on the basis of one of the auxiliary requests 1-3 filed during the proceedings before the opposition division.

XII. The respondents both request that the appeal be dismissed.

## **Reasons for the Decision**

*Main request (patent as granted)*

1. Inventive step

1.1 Closest prior art

All parties agree on the choice of document D7 as the closest prior art. The Board sees no reason to differ.

D7 generally relates to a method of making composite active particles for inhalation, comprising the steps of milling particles of the active material with particles of an additive material, so as to promote dispersion of the particles and avoid the formation of agglomerates (e.g. page 4, lines 13-18).

A disclosure of glycopyrrolate as active material can be found in example 5 of D7, where micronised glycopyrrolate and magnesium stearate (in a ratio of 75:25 or 95:5) are milled together in a mechanofusion machine.

According to the appellant, the process shown in example 5 of D7 leads to a complete and coherent coating of magnesium stearate onto the glycopyrrolate particles, with both ratios of 75:25 and 95:5. A reproduction of example 5 of D7 (i.e. D14) and two declarations (D15 and D16) were submitted as evidence. The Board sees no reason to question these conclusions.

## 1.2 Differentiating feature

Claim 1 is directed to a dry powder formulation suitable for inhalation comprising glycopyrrolate and magnesium stearate, wherein the glycopyrrolate is defined in terms of the process for its preparation, namely by micronisation followed by conditioning. The Board notes that claim 1 contains no limitation as to how the magnesium stearate is to be incorporated into the final formulation. Accordingly, the magnesium stearate may be incorporated as a coating after conditioning. Indeed, a coating step is explicitly considered in the patent in suit in example 8 (which is not identified as a reference example), where a glycopyrrolate is coated with 5% magnesium stearate in a manner similar to that of D7.

Thus claim 1 covers dry powder formulations resulting from the following sequence of steps:

- micronising glycopyrrolate,
- conditioning the micronised glycopyrrolate by exposure to humid conditions of 50-90% RH at temperatures between 10 to 50°C for at least 48 hours, and finally
- coating the conditioned micronised glycopyrrolate with magnesium stearate as in D7.

The closest prior art D7 does not disclose such a conditioning step. However, claim 1 does not relate to a process *per se*, but to the formulation resulting from this process. The question may arise as to what differentiating feature, if any, the final formulation will exhibit as a result of this intermediate conditioning step. In the following sections, the Board accepts, in the appellant's favour, that the

conditioning step results in a different formulation over the one disclosed in D7.

### 1.3 Objective technical problem

It is undebated that the claimed formulation does not exhibit any improved stability over the particles of D7 as a result of the conditioning step. The inhalable glycopyrrolate formulation of D7 is stated by the appellant (e.g. in D15) to already have excellent stability. No evidence was adduced allowing for a proper comparison between conditioned and unconditioned formulations of magnesium stearate - coated glycopyrrolate.

The Board thus concurs with the appellant's definition of the technical problem as the provision of an *alternative* formulation of stabilized glycopyrrolate and magnesium stearate suitable for inhalation.

### 1.4 Obviousness of the claimed solution

Document D8 relates to a generally applicable process for providing a stable crystalline form of a fine-grained substance or substance mixture which can be produced, stored and used while maintaining the aerodynamic properties required for inhalation (see the abstract). D8 thus belongs to the same technical field and addresses the same problem as D7 or the patent. D8 explains on page 2, lines 10-21 that micronisation of solids often leads to the formation of defects or amorphous regions, which are often more sensitive to moisture. D8 solves the problem of stability on storage by a conditioning step in which the micronised material is treated with a water containing vapour phase in a controlled fashion, under the same conditions as those

defined in claim 1 of the patent in suit, namely a temperature preferably between 10 and 50°C, a relative humidity preferably above 50%, for a time ranging from minutes to days (see page 5, line 15 to page 6, line 1). Thus D8 suggests to apply the claimed conditioning step as a solution to the same problem of stability on storage. Regarding the order of steps, D8 also considers mixing the substances after conditioning (see page 10, lines 9-11) and recommends that the conditioning step be performed directly after micronisation (see paragraph bridging pages 10-11).

Thus, in light of D8, the skilled person would anticipate that the addition of a conditioning step prior to coating as taught in D7 would still lead to stable particles. Accordingly, to the extent that the intermediate conditioning step leads to a difference in the final formulation, this difference is obvious in light of D8.

- 1.5 The appellant submits that the stability issue is already solved in D7, such that the skilled person would not subject the already stable glycopyrrolate particles to the conditioning step of D8 when there was no expectation of a benefit in doing so.

However, under the problem-solution approach, what the skilled person would or would not do has to be considered in the light of the objective technical problem, which in the present case is the provision of an alternative. The skilled person looking for alternatives to the formulations of D7 will consider modifying the preparation method disclosed therein. Furthermore, the starting material in example 5 of D7 is micronized glycopyrrolate. According to D7 (see page 4, lines 13-15), it is known that milling generates

amorphous material on the surface of the particles, making them more cohesive. Thus D7 would prompt the skilled person to address the presence of amorphous material (in the starting material of D7) by adding a conditioning step as taught in D8 before coating with magnesium stearate.

Contrary to the appellant's arguments, the skilled person has no reason to expect that the solution disclosed in D8 would not be applicable to glycopyrrolate on account of its greater hygroscopicity. D8 precisely addresses the issue of sensitivity to moisture (see page 2, lines 15-16), and presents the conditioning step as a generally applicable solution. No prejudice was shown to exist in the prior art against the application of the solution to the particular case of glycopyrrolate.

It follows from the above that the main request does not comply with the requirements of Article 56 EPC.

#### *Auxiliary requests 1-3*

#### 2. Inventive step

Auxiliary requests 1-3 (see III. above) were submitted during the first-instance proceedings. The opposition division found the subject-matter of each of these auxiliary requests not to involve an inventive step, and set out its reasons in points 2-4 of the decision under appeal.

The appellant maintains the same auxiliary requests 1-3 during the present appeal proceedings. However, on the issue of inventive step for these auxiliary requests, the appellant merely refers to his arguments set out in

respect of the main request, and is silent on the relevance of the additional features introduced in these auxiliary requests.

According to Article 12(3) RPBA 2020, the statement of grounds of appeal shall set out clearly and concisely the reasons why it is requested that the decision under appeal be reversed, amended or upheld. In the present case, the reasons submitted by the appellant are limited to those set out in respect of the main request.

In the absence of proper substantiation by the appellant regarding the additional features introduced in auxiliary requests 1-3, the Board does not see any reasons why the decision of the opposition division on these requests should not hold good and, accordingly, considers that the subject-matter of these requests does not involve an inventive step.



**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chairman:



B. Atienza Vivancos

A. Usuelli

Decision electronically authenticated