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# Datasheet for the decision of 7 October 2021

**Case Number:** T 1818/18 - 3.3.07

**Application Number:** 11755043.4

**Publication Number:** 2611423

**IPC:** A61K9/14, A61K31/58, A61P11/06, A61K31/137, A61K31/133, A61K9/00, A61J3/00, A61M15/00, B65B31/00

**Language of the proceedings:** EN

**Title of invention:**

DRY POWDER INHALATION DRUG PRODUCTS EXHIBITING MOISTURE CONTROL PROPERTIES AND METHODS OF ADMINISTERING THE SAME

**Patent Proprietor:**

GlaxoSmithKline Intellectual Property Development Limited

**Opponents:**

Oser, Andreas
Generics (U.K.) Limited
Teva UK Limited

**Headword:**

Dry powder inhalation drug products / GLAXOSMITHKLINE

**Relevant legal provisions:**
EPC R. 111(2)
EPC Art. 114(2), 54(3), 56, 83
RPBA Art. 12(4)
RPBA 2020 Art. 11, 13(1)

**Keyword:**
Substantial procedural violation - appealed decision reasoned (yes)
Late submitted material - admitted (partly)
Sufficiency of disclosure - (yes)
Novelty - (yes)
Inventive step - (yes)

**Decisions cited:**
G 0001/15

Europäisches Patentamt
European Patent Office
Office européen des brevets

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**Case Number: T 1818/18 - 3.3.07**

# D E C I S I O N
# of Technical Board of Appeal 3.3.07
# of 7 October 2021

| | |
|---|---|
| **Appellant:** (Opponent 1) | Oser, Andreas<br>Sohnckestrasse 12<br>81479 München (DE) |
| **Representative:** | Maiwald Patent- und Rechtsanwaltsgesellschaft mbH<br>Elisenhof<br>Elisenstraße 3<br>80335 München (DE) |
| **Appellant:** (Opponent 2) | Generics (U.K.) Limited<br>Station Close<br>Potters Bar<br>Hertfordshire EN6 1TL (GB) |
| **Representative:** | FRKelly<br>27 Clyde Road<br>Dublin D04 F838 (IE) |
| **Appellant:** (Opponent 3) | Teva UK Limited<br>Ridings Point<br>Whistler Drive<br>Castleford WF10 5HX (GB) |
| **Representative:** | Elkington and Fife LLP<br>Prospect House<br>8 Pembroke Road<br>Sevenoaks, Kent TN13 1XR (GB) |
| **Respondent:** (Patent Proprietor) | GlaxoSmithKline Intellectual Property Development Limited<br>980 Great West Road<br>Brentford<br>Middlesex TW8 9GS (GB) |
| **Representative:** | Billson, Siân Catherine<br>GlaxoSmithKline |

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**Decision under appeal:** **Interlocutory decision of the Opposition Division of the European Patent Office posted on 17 May 2018 concerning maintenance of the European Patent No. 2611423 in amended form.**

**Composition of the Board:**

**Chairman** A. Usuelli
**Members:** E. Duval
Y. Podbielski

## Summary of Facts and Submissions

I. European Patent 2 611 423 ("the patent") was granted on the basis of 20 claims.

Claim 1 of the patent related essentially to a drug product comprising:

- a dry powder inhalation (DPI) device containing (I) vilanterol and (II) fluticasone furoate;
- a hygroscopic material; and
- a package encompassing the DPI device and the hygroscopic material, defining an enclosed volume therein which exhibited a given Relative Humidity (RH).

Vilanterol refers to 4-{(1*R*)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy] ethoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol (or compound B, for vilanterol trifenatate).

Fluticasone furoate refers to (6α,11β,16α,17α)-6,9-difluoro-17-{[(fluoromethyl)thio]carbonyl}-11-hydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl 2-furancarboxylate (or compound A).

II. Three 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 as filed.

III. The opposition division took the interlocutory decision that, on the basis of the main request filed by letter dated 19 February 2018, the patent met the requirements of the EPC.

Claim 1 of the main request read as follows:

"A drug product comprising:
a dry powder inhalation device containing one or more pharmaceutical compositions present therein, wherein the one or more pharmaceutical compositions comprise active ingredients (I) 4-{(1*R*)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol, or a salt thereof, and (II) (6α,11β,16α,17α)-6,9-difluoro-17-{[(fluoromethyl)thio]carbonyl}-11-hydroxy-16-methyl-3-oxoandrosta-1,4-dien-17-yl 2-furancarboxylate or a solvate thereof;
a hygroscopic material; and
a package which encompasses the dry powder inhalation device and the hygroscopic material defining an enclosed volume therein;
wherein each of the active ingredients (I) and (II) are present in the same or different pharmaceutical compositions, and wherein the enclosed volume within the package exhibits a Relative Humidity of from 20% to 40%."

IV. The decision of the opposition division cited among others the following documents:

D1: WO 03/024439 A1
D8: WO 2009/013244 A1
D9: Vaczek D. "Dialing in stable packaging for sensitive drugs", Pharmaceutical & Medical Packaging News, Category: "Desiccants", July 1, 2010.
D11: Guidance for industry, "Metered dose inhaler (MDI) and dry powder inhaler (DPI) drug products", draft guidance, US Department of Health and Human Services,

Food and Drug Administration, Center for Drug Evaluation and Research (CDER), October 1998
D12: WO 2007/109606 A2
D13: WO 2008/040841 A1
D14: Telko et al, "Dry powder inhaler formulation", Respiratory Care, September 2005, Vol 50, No. 9, pp 1209-1227
D15: Lehto et al. "Moisture transfer into medicament chambers equipped with the double-barrier-desiccant system" International Journal of Pharmaceutics 275 (2004 ), pp 155-164
D16: EP 2954888 A1
D17: WO 01/98174 A1
D20: Multisorb Online Publication dated July 2007
D25: Aulton. The Science of Dosage Form Design, Pharmaceutics:
Second edition 2002, pp 379-382
D26: "A Guide to the Measurement of Humidity", Institute of Measurement and control, National Physical Laboratory, 1996
D27: "A beginner's guide to humidity measurements, National
Physical Laboratorv, October 2011
D28: User Guide for the HygroPalm meter from Rotronic
D33: Zeng et al. "Particle interactions in dry powder formulations for inhalation", Taylor & Francis, London, 2001. Chapter 5
D35: Physician's Desk Reference, Thompson Reuters, 63rd edition, 2009, pages 1276-1288, 1435-1440 and 1594-1601
D36: experimental data showing impact of temperature on relative humidity (filed on 19 February 2018)
D37: extract from the regulatory dossier for RELVAR™ ELLIPTA™
D38: RELVAR™ ELLIPTA™ device

V. In particular, the opposition division decided that:

(a) D36-D38 were admitted into the proceedings

(b) The subject-matter of the main request was sufficiently disclosed. Although the patent did not indicate the temperature at which the RH was measured, this temperature was assumed to be the room temperature.

(c) The main request validly claimed priority, such that D16 was not part of the prior art under Article 54(2) EPC.

(d) D1 was chosen as the closest prior art. The distinguishing features were the presence of a package, a desiccant comprised in the package, and the RH of 20-40% of the enclosed volume within the package. This resulted in a stabilisation of the fine particule mass (hereinafter FPM) of both fluticasone and vilanterol in the drug combination product. The objective technical problem was the provision of an improved DPI device containing fluticasone and vilanterol wherein the FPM is stable. The claimed solution was not obvious in light of the cited prior art.

VI. Each of opponent 1 (appellant 1), opponent 2 (appellant 2) and opponent 3 (appellant 3) lodged an appeal against the decision of the opposition division.

With its statement setting out the grounds of appeal, appellant 1 filed A001-A003:

A001: WO 2010/135340

A002: World Health Organization, WHO Technical Report Series, No. 953, 2009, Annex 2: Stability testing of active pharmaceutical ingredients and finished pharmaceutical products
A003: Submission dated 24 April 2015 in the European patent application No. 11 755 042.6 filed by the same Applicant

VII. In its reply to the appeals dated 4 February 2019, the patent proprietor (respondent) defended its case on the basis of the main request submitted on 19 February 2018 and upheld by the opposition division. It additionally filed auxiliary requests 1-5.

VIII. Appellant 3 submitted further arguments in its letter dated 11 April 2019. By letter dated 20 May 2020, appellant 3 filed A004 and A005:

A004: Declaration of David Howlett dated 1 May 2020
A005: CV of David Howlett ("Exhibit 1" in the declaration)

IX. The Board set out its preliminary opinion in a communication under Article 15(1) RPBA issued on 3 June 2020.

X. Further submissions were made by appellant 3 in a letter dated 15 June 2020, by the respondent on 21 August 2020, by appellant 3 on 15 September 2020 and 11 May 2021, by appellant 1 on 5 August 2021, and by appellant 2 on 4 October 2021.

XI. On 7 October 2021, oral proceedings were held before the Board.

XII. The arguments of the appellants can be summarised as follows:

(a) Insufficient reasoning in the appealed decision

The decision under appeal did not address the objection, which opponent 2 had raised, of lack of inventive step over D1 in combination with D13. Hence, the appealed decision was insufficiently reasoned within the meaning of Rule 111(2) EPC.

(b) Admittance of D37 into the proceedings

During the opposition proceedings, the patent proprietor had filed document D37 late without justification and despite the fact that it had known of D37 for a long time. In addition, D37 was not *prima facie* relevant. Thus the opposition division did not correctly exercise its discretionary power when admitting of D37.

(c) Admittance of A004-A005 into the appeal proceedings

The submissions of 20 May 2020, including A004/A005, had to be read together with those of 11 April 2019 as a legitimate attempt to answer the respondent's objections to the grounds for appeal. A004/A005 were filed before the preliminary opinion of the Board, contained no new experimental evidence, and were *prima facie* relevant. Hence, A004/A005 should be admitted.

(d) Main request, sufficiency of disclosure

Claim 1 related to a drug product defined by a RH of 20-40% for the enclosed volume within the package. According to established case law, a reliable method

for measuring that parameter had to be provided in the patent or be part of the common general knowledge. However, the patent was silent on the temperature for the measurement of RH. This temperature had an effect on RH, as shown in D25-D28. Thus, the criteria of sufficiency of disclosure were not met.

(e) Main request, novelty

The subject-matter of the main request was not directly and unambiguously derivable from the priority application and was therefore not entitled to the priority date. As a consequence, the claimed subject-matter lacked novelty over D16, prior art under Article 54(3) EPC to the extent that the priority was invalid.

(f) Main request, inventive step

The closest prior art D1 disclosed combinations of fluticasone and vilanterol for use in a DPI. The subject-matter of claim 1 differed by:
a) the presence of a package;
b) a hygroscopic material provided within the package; and
c) the RH of 20-40% of the enclosed volume within the package.

The adjustment of humidity had no effect as far as Vilanterol was concerned. As to fluticasone furoate, neither the figure of the patent nor D37 showed that an improvement in FPM stability was consistently associated with the claimed range. Furthermore, any effect shown using a silica gel desiccant pack with a RH of 20-30% did not plausibly arise over the whole scope of the claim. If an effect could be attributed over D1, it was to be expected considering the general

knowledge reflected in D11, D14 and D15. There was no synergistic effect between the package and the hygroscopic material.

The objective technical problem was either the provision of an alternative product, or of a further DPI with fluticasone furoate and vilanterol as APIs with a suitable FPM adjustment, or where the FPM was stable.

The claimed solution did not involve an inventive step in light of D8, D9, D11, D12, D13, D15, D17, D20, D33 and D35.

According to the guidance for DPI products D11, the provision of a DPI product with protective packaging was a standard measure, and the stability problems induced by moisture in DPI formulations had to be investigated. Hence, starting from D1 and following the standards required by D11, a skilled person would have had to test and then inherently arrive at a RH range suitable for the drug formulation of fluticasone furoate and vilanterol in the course of routine experimentation. The skilled person would be prompted by D9 to select a suitable desiccant package.

The skilled person would receive further motivation to enclose a desiccant in the package from D8, showing that the control of RH in the package enclosing the DPI by a suitable desiccant effectively protected DPI compositions, and from D12, mentioning that a desiccant pack enabled the absorption of ingressive moisture, such as silica gel which maintained a RH of 10-30%.

D13 addressed the problem of FPM stability in DPIs and suggested that maintaining a relatively low and

constant humidity improved the stability of the formulation, e.g. by placing the DPI in an impermeable container together with a conventional desiccant pack such as silica gel.

D15 taught the use of a barrier packaging and a desiccant to control RH. D17 pointed generally to the provision of a desiccant in the packaging to maintain the stability of the dry powder formulation over time. D33 emphasised the importance of humidity control in handling and storage of dry powder aerosols, and pointed to adding a desiccant inside the packaging to improve the stability of the product against environmental moisture. The specific range of 20-40% would have resulted from routine experimentations. D35 also showed that DPI devices were routinely stored in plastic-coated, moisture protective foil pouches as standard practice. D20 further showed that inserting the DPI in a secondary package together with the desiccant belonged to the common general knowledge. The skilled person would have had a strong incentive to adjust RH in reasonable expectation of attaining a stabilization of the FPM of the active ingredient in the DPI device.

XIII. The respondent's arguments can be summarised as follows:

(a) Admittance of D37 into the proceedings

The opposition division had exercised their discretionary power correctly. In light of the relevance of D37, it was appropriate that this document was admitted into the proceedings.

(b) Admittance of A001-A005 into the appeal proceedings and remittal to the opposition division

A001, submitted only at appeal stage and used as the basis of a new inventive step argument, was not *prima facie* highly relevant, and should thus not be admitted into proceedings. In the event that A001 was admitted into the proceedings, the case should be remitted to the opposition division for further examination.

A002 and A003, submitted late by appellant 1 without justification, should not be admitted into proceedings either.

A004/A005 predominantly concerned an assessment of the data included in the patent and discussed at length in the proceedings before the opposition division. A004/ A005 should have been submitted during the first instance proceedings. No reason had been provided for their very late submission, contrary to Article 13(1) RPBA 2020.

(c) Admittance into the appeal proceedings of the inventive step objections submitted for the first time with the grounds of appeal of appellants 1, 2 and 3

Appellants 1, 2 and 3 had raised for the first time in their respective grounds of appeal new arguments regarding inventive step based on new combinations of the cited art. Since the appeal proceedings should constitute a review of the appealed decision and not a re-run of the opposition proceedings, these arguments were not to be admitted into the proceedings

(d) Main request, sufficiency of disclosure

In absence of a specified temperature, the RH measurements would be made at room temperature. This was accepted practice and logical, since storage of such products also took place at room temperature. Furthermore, D36 demonstrated that variations in room temperature (i.e. from 20°C to 25°C) had no significant impact upon the RH measured in the drug product claimed. Hence the criteria of sufficiency of disclosure were met.

(e) Main request, novelty

The objection of lack of novelty under Article 54(3) EPC over the published divisional application D16 of the patent was irrelevant in light of G 1/15.

(f) Main request, inventive step

D1 related to a combination of vilanterol and e.g. fluticasone furoate formulated for inhalation. The DPI device of D1 was a naked product, i.e. the inhaler was not packaged. The subject-matter of claim 1 of the main request differed by a) a package encompassing the DPI device and b) a hygroscopic material comprised in said package which maintained the RH environment of 20-40% RH in the enclosed volume.

As shown in the patent and in D37, the distinguishing features had a profound effect on the stability of fluticasone furoate. The objective technical problem was the provision of a drug product comprising vilanterol and fluticasone furoate, wherein the FPM is stable.

The guidance D11 merely referred broadly to a study to assess the effect of different environmental conditions such as humidity, but did not refer to any desiccant system, ranges of RH or how to control these ranges. D9 did not teach to use a drop-in desiccant as a primary desiccant system in the package encompassing the device, but as a secondary one, the primary system being contained in the device itself. D8 was limited to pulverulent preparations of different medicaments and would thus not have been considered by the skilled person when seeking a solution. D12 outlined different means for managing moisture than those of the present invention, namely a desiccant entrained plastic, and did not teach a RH range of 20-30% but considered also low RH. D17 pointed to the absorption of any residual moisture and thus to low RH. The desiccant packs used in the invention were considered unsuitable in D13 for the desiccant system shown therein, and D13 did not teach a RH of 20-40%. D15 also disclosed a completely different desiccant system, namely a double-barrier-desiccant system. D33 merely taught to incorporate a desiccant inside the device rather than the packaging, and provided no teaching with regard to RH. D35 did not disclose any desiccant system at all.

Hence the criteria of inventive step were met.

XIV. Each of appellant 1, appellant 2 and appellant 3 request that the decision under appeal be set aside and that the patent be revoked in its entirety. Appellant 1 contests the opposition division's decision to admit D37 into the proceedings, and appellant 2 objects that the decision is not sufficiently reasoned within the meaning of Rule 111(2) EPC.

XV. The respondent requests that the patent be maintained on the basis of the main request submitted on 19 February 2018 and upheld by the opposition division, or, alternatively, on the basis of one of auxiliary requests 1-5 filed with letter dated 4 February 2019.

The respondent further requests that:
- A001 to A003 submitted by appellant 1, and
- A004, A005 and the corresponding submissions of appellant 3 dated 15 June 2020
not be admitted into the proceedings.

In the event that the Board is minded to admit A001 to A005 into proceedings, the respondent requests that the case be remitted to the opposition division. In addition, the respondent requests that those inventive step objections which were submitted for the first time with the grounds of appeal of appellants 1, 2 and 3 not be admitted into the appeal proceedings.

## Reasons for the Decision

1. Objection of insufficient reasoning in the appealed decision

1.1 During the proceedings before the opposition division, appellant 2 (then opponent 2) raised an objection of lack of inventive step over D1 in combination with D13. According to appellant 2, this objection is acknowledged in the appealed decision (see paragraph 12.11), but is not addressed anywhere in the decision. As a result, the appealed decision would not be sufficiently reasoned within the meaning of Rule 111(2) EPC.

1.2 The Board does not share this opinion.

The decision under appeal addresses the objection of lack of inventive starting from D1 as closest prior art, and formulates the problem as the provision of an *improved* DPI device containing fluticasone and vilanterol wherein the FPM is stable. The decision acknowledges the objections raised by the opponents, including the objection based on a combination of D1 and D13, and indicates that, according to opponent 2, D13 pertains to the common general knowledge and is concerned with the control of moisture content of DPI formulations (see paragraph 12.11). The opposition division then reasons that the opponents' objections are based on an alleged lack of any effect and on a problem formulated as the provision of an alternative. In contrast, the opposition division considers that the differentiating features over D1 result in a particular technical effect, namely the stabilisation of the FPM of both fluticasone and vilanterol in the drug combination product (see paragraphs 12.7, 12.8, 12.13, 12.14).

Even though the decision omits to analyse D13 in more detail, it can be inferred from the opposition division's reasoning that it did not consider that D13 taught the particular technical effect acknowledged for the claimed subject-matter.

1.3 Thus, the appealed decision is sufficiently reasoned as required by Rule 111(2) EPC.

2. Admittance of D37 into the proceedings

2.1 The opposition division exercised its discretion and admitted D36-D38, in particular D37, into the

proceedings. Appellant 1 challenges the opposition division's decision to admit D37.

2.2 The Board however notes that, since D37 was admitted by the opposition division, it has become part of the opposition proceedings. Furthermore, all parties have commented on D37 in their statements setting out the grounds of appeal. Under these circumstances, neither the RPBA nor Article 114(2) EPC provide any basis for excluding or otherwise disregarding D37 in the appeal proceedings.

3. Admittance of A001-A005 into the appeal proceedings and remittal to the opposition division

3.1 Together with its statement of grounds of appeal, appellant 1 submitted A001-A003. The respondent requests that these documents not be admitted into the appeal proceedings.

3.1.1 Since appellant 1's statement of grounds of appeal was submitted before 1 January 2020, Article 12 paragraphs (4)-(6) RPBA 2020 do not apply. Rather, the question whether or not A001-A003 should be admitted must be decided on the basis of Article 12(4) RPBA 2007 (Article 25(2) RPBA 2020). Article 12(4) RPBA 2007 gives the Board discretion not to admit, on appeal, documents that could have been presented in the opposition proceedings.

3.1.2 Appellant 1 relies on A001 as closest prior art in a new objection of lack of inventive step. No justification was offered for filing A001 only on appeal. The Board underlines that the appeal proceedings are not about bringing an entirely fresh

case. Accordingly, the Board did not admit A001 into the proceedings, pursuant to Article 12(4) RPBA 2007.

3.1.3 In contrast, A002 is seen as an appropriate reaction to developments in the previous proceedings. A002 was filed by appellant 1 to further support the objection of lack of inventive step starting from D1 raised during the proceedings before the opposition division. For this reason, the Board admitted A002 into the proceedings.

3.1.4 The Board however does not see the admission of A002 as a special reason, in the sense of Article 11 RPBA 2020, for remitting the case to the opposition division, because this document does no result in a case substantially different from that decided at first instance.

3.1.5 A003 was filed to substantiate appellant 1's argument that D37 should have been submitted earlier. Given the Board's finding that D37 is part of the proceedings (see 2.2 above), the relevance of A003 is moot. Accordingly, the Board did not admit A003 into the proceedings.

3.2 Appellant 3 introduced documents A004 and A005 with its letter dated 20 May 2020, and filed further submissions based on A004/A005 in its letter dated 15 June 2020. A004 and A005 consist in a declaration from an expert and his *curriculumn vitae*. The declaration A004 analyses the examples of the patent in particular as regards the different initial (INT) FPM values shown therein.

Since this evidence was submitted after the filing of the grounds of appeal, Article 13(1) RPBA 2020 applies,

in addition to Article 12(4) RPBA 2007. The Board agrees with the respondent that this analysis of the data in the patent could and should have been submitted earlier. The filing of A004/A005 is not responsive to any particular development in the proceedings.

Accordingly, the Board decided not to admit A004 and A005 and the submissions of 15 June 2020 as far as they rely on A004 and A005 as evidence.

4. Admittance into the appeal proceedings of the inventive step objections submitted for the first time with the grounds of appeal of appellants 1, 2 and 3

4.1 The respondents considers that several arguments of lack of inventive step presented on appeal by the appellants are based on new combinations of the cited art and should not be admitted into the proceedings.

4.2 In the Board's view, these objections are based on the same closest prior art (D1) in combination with documents already cited in the context of inventive step in the proceedings before the opposition division. These objections are seen as an appropriate reaction to the decision under appeal. Furthermore, some of the objections on appeal of appellants 2 and 3 are not new objections since they were already raised by appellant 1 in the previous proceedings.

4.3 Consequently, the Board admitted these objections into the proceedings.

5. Main request

5.1 Sufficiency of disclosure

5.2 Claim 1 relates to a drug product defined *inter alia* by a parameter, namely by a RH of 20-40% for the enclosed volume within the package. Appellant 3 considers that the RH is not sufficiently disclosed if a temperature is not specified in the patent for the measurement.

5.3 To examine sufficiency of disclosure for the subject-matter of claim 1 of the main request, the Board assesses below:
- whether, and to what extent, the lack of indication of the temperature for the measurement may lead to variation in the RH measured, and
- whether this ambiguity regarding the RH parameter, if present, is such that the skilled person, based on the whole disclosure of the patent and on his common general knowledge, is not able to carry out the claimed invention.

5.4 Regarding the first aspect, RH is defined as percentage ratio of the water vapour pressure to the saturation (or 100%) water vapour pressure at the same temperature. As generally indicated in D25, if the temperature is raised, then the air will be able to take up more moisture (i.e. the 100% value will increase) and the RH falls. D26 (see page 10, section 4.1), as well as D27 and D28, also emphasize the importance of the temperature in the measurement of RH and give some estimations of the influence of change in temperature on measured RH.

Appellant 3 is of the opinion that this general principle applies also in the case of a closed system

including a desiccant: in a closed system like a pack, the amount of water is fixed but the RH will still vary with the measurement temperature. However, in the Board's view, there is no evidence that, in such a closed system including a hygroscopic material, the amount of water present as vapour will not vary with the measurement temperature. Accordingly, it cannot be clearly concluded from D25-D28 to what extent, if any, a variation in the measurement temperature may influence the measured RH in the particular case of an enclosed volume comprising the hydroscopic material within the package.

5.4.1 D36 is also inconclusive regarding the influence of measurement temperature on the RH measured for a given product or sample: in D36, different samples have their RH measured at different temperatures (the samples stored at 20°C have their RH measured at 20°C, and the samples stored at 25°C have their RH measured at 25°C).

5.4.2 Thus the evidence on file does not allow to draw any conclusion as to the influence of temperature on the measured RH in the context of the claimed products.

5.5 As to the second aspect, appellant 3 referred to the passages of the Case Law of the Boards of Appeal of the European Patent Office corresponding, in the 9th edition 2019, to II.C.5.5 and II.C.8.2. In connection with this aspect, the Board considers that appellant 3's objection regarding the missing indication of the measurement temperature rather pertains to the criteria of clarity. Appellant 3 has not shown why this alleged lack of clarity of the RH parameter should lead to a finding of insufficiency of disclosure. To the extent that the lack of indication of a measurement temperature would render the RH parameter ambiguous or

ill-defined, it is not shown that, as a result of this ambiguity, the skilled person, based on the whole disclosure of the patent and on his common general knowledge, is not able to carry out the claimed invention.

5.6 Accordingly, the criteria of sufficiency of disclosure are fulfilled.

6. Novelty - priority

6.1 The appellants are of the opinion that the subject-matter of the main request is not directly and unambiguously derivable from the priority application and is therefore not entitled to the priority date. Appellant 2 argues that, as a consequence, the claimed subject-matter lacks novelty over D16, prior art under Article 54(3) EPC.

6.2 D16 is a published divisional application filed in respect of the application from which the patent was issued. It claims the same priority as the patent in suit. Following G 1/15, to the extent that D16 discloses any subject-matter encompassed by the claims of the main request, and that this subject-matter is disclosed in the priority application, then the main request is entitled to priority in respect of that subject-matter. The objection of lack of novelty over D16 is thus unconvincing.

7. Inventive step

7.1 Claim 1 of the main request relates to a drug product comprising:
- a DPI device containing one or more pharmaceutical compositions, wherein the composition(s) comprises

(I) vilanterol, and
(II) fluticasone furoate;
- a hygroscopic material; and
- a package which encompasses the DPI device and the hygroscopic material defining an enclosed volume therein;
further defined in particular in that the enclosed volume within the package exhibits a RH of 20-40%.

The invention aims at controlling the humidity within the DPI device and hence the FPM (see paragraph [0006] of the patent). According to the patent (see paragraph [0010]), "the drug product is capable of exhibiting improved shelf life and more stable fine particle mass as a result of the Relative Humidity with the package enclosed volume being controlled within a specified range".

7.2 All parties regard D1 as a suitable starting point for the assessment of inventive step. The Board sees no reason to differ.

D1 discloses a dry powder formulation of vilanterol in combination with a corticosteroid such as fluticasone furoate (see page 13, lines 17-18; page 16, lines 6-8 and 30; claims 6 and 9; page 17, lines 11-13). This dry powder composition is suitable for topical delivery to the lung by inhalation (see page 25, last paragraph), for instance in form of an inhaler, i.e. a DPI device such as the Rotahaler, Diskus, Diskhaler or Turbuhaler. D1 mentions a packaging of the formulation (i.e. for use in the DPI device), but does not mention a packaging encompassing the DPI device itself. The content of D1 does not make implicit the presence of such a secondary packaging either. As summarized by the opposition division, D1 thus discloses a DPI device

without a secondary wrapping or package and without a desiccant, i.e. D1 discloses a "naked" product as referred to in the patent (see paragraph [0081], page 13 line 50).

7.3 The drug product of claim 1 differs from the product of D1 in that it further comprises:
- a hygroscopic material and
- a package encompassing the DPI device and the hygroscopic material defining an enclosed volume therein,
and in that the enclosed volume within the package exhibits a RH of 20-40%.

7.4 Turning to the technical effect associated with the above differentiating features, the Board accepts that the data represented in example 3 and figures 12, 14 and 16 suitably demonstrate an effect on the FPM of fluticasone furoate associated with the differentiating features in combination.

7.4.1 In example 3, dry powder blends containing respectively vilanterol trifenatate (25 µg) and fluticasone furoate (50 µg, 100 µg or 200 µg) were separately packaged in strips and one strip of each active was incorporated into a DPI device. The data compare the FPM of fluticasone furoate (i.e compound A) in DPI devices stored naked (i.e. stored without overwrap or desiccant as per D1) or stored overwrapped with a desiccant package with a RH of either 10%, 15%, 20%, 30% or 40%. An effect on stabilisation of the FPM of fluticasone furoate can be observed when the samples are subjected to accelerated storage conditions (25°C and 60% RH, and 40°C and 75% RH). For naked products, the FPM of fluticasone furoate drops off significantly in comparison with products stored overwrapped with a

desiccant and having a RH as claimed in the enclosed volume (OW+D).

The Board agrees with the appellants that vilanterol remains, in comparison, essentially unaffected by humidity conditions, such that no improvement in respect of vilanterol is to be taken into account.

7.4.2 Thus, an effect is shown to arise from the differentiating features taken together (namely the hygroscopic material, the package and the RH of 20-40%). The parties additionally debated which of the individual differentiating features accounted for the effect. In the Board's opinion, figures 12, 14 and 16 show that the samples with the least variation of FPM are those with a RH in the claimed range (namely OW+D(20), OW+D(30) and OW+D(40), in comparison with e.g. OW+D(15)), thus demonstrating that the RH range does contribute to the achievement of the improved FPM stability, and that the effect does not merely result from the packaging.

7.4.3 The remaining figures of the patent, and D37, do not compare a naked product with a product as claimed, and hence cannot modify the above conclusion regarding the effect resulting from the differentiating features taken together.

Furthermore, the contribution of the claimed RH range to the effect is not contradicted by figures 1-6, because these figures do not compare a claimed product with one having a RH outside the range. As to figures 9 and 10, products with a desiccant and a RH in the claimed range also exhibit better FPM stabilities than products with a RH outside that range.

The above conclusions are also not modified by the differences in FPM distribution at the beginning of each test (abbreviated INT) pointed out by the appellants. This is because the variations in initial FPM values remains small in comparison with the FPM drop in the naked product or the product with a RH outside the claimed range. As such, they do not call into question the effect observed. Furthermore, the respondent explained these variations by the fact that, in example 3, each product was analysed before being placed in storage in stability chambers. Thus, these variations do not indicate that the samples were prepared differently or would differ by any other feature than the above differentiating features.

7.4.4 The appellant expressed the view that the above effect did not arise over the whole scope of claim 1, because claim 1 was not limited as regards the nature of the packaging and of the hygroscopic material, its hydration level and / or the RH of the desiccant pack.

The Board does not share this view. The package and hygroscopic material are limited as a consequence of the further features of claim 1. Thus, since claim 1 requires that the package define an enclosed volume with a defined RH, it rules out packages which would be unable to do so, such as a mere cardboard package. Likewise, claim 1 covers products with desiccant types, amounts or hydration levels only in as far as they lead to the RH in the enclosed space defined in claim 1. In light of the data in the patent, these controlled humidity conditions in the enclosed volume credibly lead to the effect on FPM. The appellants did convincingly show that particular desiccants could fail to have the observed effect on FPM even though the RH in the enclosed space is as claimed. For instance, it

can be expected that the use of dry silica as hygroscopic material will cause the RH in the enclosed volume to drop below the lower limit of 20%. Accordingly, it is not relevant whether such a product fails to achieve the improved FPM stability, because this product does not fall anymore within the scope of claim 1. Likewise, if the hygroscopic material is incorporated in such small amounts that it cannot control the RH within the claimed range, then the product falls outside the scope of the claim.

7.5 Consequently, the objective technical problem is the provision of a drug product comprising vilanterol and fluticasone furoate, wherein the stability of the fluticasone furoate FPM is improved.

7.6 For the following reasons, the Board concludes that the claimed solution involves an inventive step.

It was generally known that, depending on their composition, DPI formulations may be hygroscopic and take up moisture, which may affect the particle size distribution and stability of the drug substance (see the general guidance D11 regarding DPI devices, page 7, lines 212-215). An evaluation of the effect of storage and of moisture equilibration on particle size distribution was required (see D11, page 50, lines 1589-1592; page 51, lines 1616-1622). Furthermore, packaging DPI devices was usual (see D11, page 4, lines 113-114). However, the general guidance D11 neither refers to any desiccant system, nor to suitable RH ranges for the enclosed volume. In this sense, D11 may require that the potential issues be investigated, but it does not provide the claimed solution.

The cited prior art does not teach that the observed improvements in FPM stability could be achieved by incorporating a hygroscopic material in the package and controlling the RH to 20-40% in the enclosed volume, whether as a general solution or in the context of fluticasone furoate. While some prior art generally indicates that DPI products should neither get too wet nor too dry (see D9, page 2), without indication of what ranges of RH would be suitable for the enclosed volume, other prior art documents point to the absorption of any residual moisture and thus to low RH (see D17, page 20). Likewise, D12 generally proposes, by means of a package composed of a desiccant-entrained plastic, to control the RH to less than 10% just as much as it suggests a RH of 10-30% (see page 5, fourth paragraph). D13, which relates to desiccant systems for protecting inhalers or powder formulations from moisture, aims at maintaining a relatively low and constant humidity in the environment surrounding the powder formulation (see page 3, last paragraph, and page 4, first paragraph), but does not point to the range of 20-40% either. Similarly, D15 (see page 156, left), D20, D33 (see pages 145, 146 and 164) and D35 are silent about the range of 20-40% RH in the volume enclosed by the package. In addition, D15 pertains to a different desiccant system, namely a double-barrier-desiccant system in which the desiccant is inside the medicament (powder) chamber (see page 157 and figure 1), and considers a RH of 30-60% inside the medicament chamber but not inside the enclosed volume.

Thus the prior art cited by the appellants does not suggest to the skilled person that the issues of FPM stability would arise in the same way and could be addressed by the same means for all DPI formulations. As stated in D33 (see page 164), dry powders may have

different sensitivities to the environmental humidity, depending not only on the excipient but also on the drug. This is confirmed by the significantly different behaviors of vilanterol and fluticasone furoate in the claimed products (see 7.4.1 above). Accordingly, D8, which related to preparations in powder form of different medicaments (namely tiotropium and salmeterol), would not have been considered by the skilled person when seeking a solution to the stability issue of fluticasone furoate.

It also follows from the above that the relationship between RH in the enclosed volume and FPM stability in the context of fluticasone furoate was not known to the skilled person. There was in particular no clear teaching that, for such a compound, a low RH would be detrimental. As a consequence, the effect brought about by the claimed range of 20-40% RH cannot be dismissed as being the mere result of routine experimentations or parameter optimisation.

Accordingly, the main request meets the criteria of inventive step.

**Order**

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

The appeals are dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated