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Datasheet for the decision of 23 February 2021

Case Number: T 2015/20 - 3.3.07

Application Number: 15173011.6

Publication Number: 2954891

IPC: A61K9/14, A61K9/72, A61K31/46, A61K45/06, A61K9/00

Language of the proceedings: EN

Title of invention:
INHALATION COMPOSITION CONTAINING ACLIDINIUM FOR TREATMENT OF ASTHMA

Applicant:
Almirall, S.A.

Headword:
Aclidinium for treatment of asthma/ALMIRALL

Relevant legal provisions:
EPC Art. 83, 56
Guidelines for examination F-III, 1

Keyword:
Sufficiency of disclosure - (yes)
Inventive step - (yes)

Decisions cited:
T 0609/02, T 0792/00, T 1164/11, T 1273/09, G 0001/03, T 1329/04, T 0488/16, T 0939/92, T 0964/92, T 0532/06, T 1677/11, T 1063/06, T 0694/92, T 0409/91, T 0014/83, T 2220/14, T 0544/12, T 0435/91

Catchword:
Claims in patent applications typically involve generalisations which inherently include an aspect of speculation. Patent applications in the field of medicine represent in this respect no exception. The approaches developed in the jurisprudence of the Boards of Appeal of the EPO for the assessment of sufficiency of disclosure and inventive step specifically take account of the technical contribution actually disclosed in a patent application to avoid patent protection resulting from unreasonable speculation on the basis of propositions that are prima facie implausible (see also points 2.6, 2.7 and 5 of the Reasons).

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Case Number: T 2015/20 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 23 February 2021

Appellant: (Applicant)	Almirall, S.A. Ronda del General Mitre 151 08022 Barcelona (ES)
Representative:	J A Kemp LLP 14 South Square Gray's Inn London WC1R 5JJ (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 20 July 2020 refusing European patent application No. 15173011.6 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	A. Jimenez

Summary of Facts and Submissions

I. The appeal was filed by the applicant (hereinafter: "the appellant") against the decision of the examining division to refuse the European patent application 15173011.6 (hereinafter: "the application"), which had been filed as divisional application with respect to European patent application 09719213.2.

II. The appealed decision was based on a single request filed on 17 December 2018. Claim 1 of this request related to:

"A pharmaceutical composition comprising aclidinium in the form of a dry powder of a pharmaceutically acceptable salt in admixture with a pharmaceutically acceptable dry powder carrier, providing a metered nominal dose of aclidinium equivalent to 400 µg (plus/ minus 10%) aclidinium bromide for use by inhalation in the treatment of asthma."

III. The decision under appeal cited the following documents:

D1: WO 2005/115465

D2: G. JOOS ET AL.: "Bronchodilator effects of aclidinium bromide, a novel long-acting anticholinergic, in COPD patients: a phase II study", 16 September 2007 (2007-09-16), pages 209S-210S, XP002487868, Retrieved from the Internet: URL:http://www.ersnet.org/learning_resources_player/abstract_print_07/files/138.pdf [retrieved on 2008-07-10]

D3: WO 02/36106

D4: SINGH D ET AL: "A randomised, placebo- and active-controlled dose-finding study of aclidinium bromide administered twice a day in COPD patients", PULMORNARY PHARMACOLOGY & THERAPEUTICS, vol. 25, no. 3, 29 March 2012 (2012-03-29), pages 248-253 ISSN: 1094-5539, DOI: 10.1016/J.PUPT.2012.03.008

D5: KJELL LARSSON: "Aspects on pathophysiological mechanisms in COPD", JOURNAL OF INTERNAL MEDICINE, vol. 262, no. 3, 1 September 2007 (2007-09-01), pages 311-340, XP055347678, GB ISSN: 0954-6820, DOI: 10.1111/j.1365-2796.2007.01837.x

D6: Anonymous: "Duaklir Genuair 340 micrograms /12 micrograms inhalation powder", www.medicines.org.uk, 5 March 2018 (2018-03-05), pages 1-14, XP055575534, Retrieved from the Internet: URL:https://www.medicines.org.uk/emc/product/3562/smpc/print [retrieved on 2019-03-28]

IV. According to the decision under appeal the application did not meet the requirement of Article 83 EPC for the following reasons.

The application did not provide any kind of evidence reflecting the therapeutic effect on which the therapeutic application of the treatment of asthma relied, whether in the form of in vitro results, in vivo pre-clinical research or results of clinical trials, which made it credible that asthma could be treated with a metered nominal dose of 400 µg aclidinium by inhalation.

Example 1 of the application as well as the post-published document D4 only demonstrated effectiveness in treatment of COPD. However, it was part of common knowledge, as evidenced by for instance document D5, that COPD and asthma were different diseases with different mechanisms involved. The results obtained in example 1 relating to treatment of COPD patients could therefore not render treatment of asthma with a metered nominal dose of 400 µg aclidinium by inhalation (or by inhalation of another dose of aclidinium for that matter) plausible.

Moreover, document D6 explicitly warned that the inhalation powder "Duaklir Genuair", which contained 396 micrograms of aclidinium bromide and 11.8 micrograms of formoterol fumarate dihydrate, should not be used in asthma and that clinical studies of Duaklir Genuair in asthma had not been conducted. Document D6 was published in 2018. It thus appeared that at the priority date of the present invention, and even in 2018, no clinical studies of a composition according to the claims had been performed which could make it credible that it has therapeutic activity in asthma.

Section II.C.5.3 of the Case Law of the Boards of Appeal of the EPO, 9th Edition 2019 indicated that an invention was in principle sufficiently disclosed if the application indicated at least one way enabling the person skilled in the art to carry out the invention. However, section II.C.7.2 of the Case Law of the Boards of Appeal, *supra*, further explained that where the therapeutic effect represented a functional technical feature of the claim, the application had to disclose the suitability of the product to be manufactured for the claimed therapeutic application. Accordingly, for a therapeutic application to be accepted as sufficiently

disclosed, the application or the common general knowledge had to provide some information rendering it technically plausible for the skilled person that the claimed compound can be applied for the claimed therapeutic use.

Sufficiency of disclosure was to be shown to exist at the effective date of a patent application. As neither the application nor the prior art provided any evidence or disclosure that rendered effective treatment of asthma with aclidinium technically plausible, the application did not disclose a plausible technical concept for the treatment of asthma. Moreover, the warning in document D6 against the use of "Duaklir Genuair" gave actually rise to serious doubts that the claimed treatment of asthma could be put into practice.

Accordingly, the application failed to sufficiently disclose the claimed invention.

V. The appellant's arguments submitted with the grounds of appeal are represented as follows.

The claims of the main request related to the use of a metered nominal dose of 400 µg aclidinium in the treatment of asthma.

All that should be necessary in order to satisfy the requirements of Article 83 EPC was that a skilled person should be able, using his or her common general knowledge and the information in the description, to prepare the specified product and to administer it to patients suffering from the specified indication. This was clearly the case in the present application as it was well within the capabilities of the skilled pharmaceutical chemist to provide a pharmaceutical

composition comprising aclidinium, which provided the required nominal metered dose of aclidinium equivalent to 400 µg aclidinium bromide, for use by inhalation in the treatment of asthma.

No serious doubts that the claimed treatment of asthma can be put into practice could be based on document D6, which presented a summary of product characteristics for Duaklir Genuair 340 micrograms / 12 micrograms inhalation powder. This document, stated in section 4.4 that "Duaklir Genuair should not be used in asthma; clinical studies of Duaklir Genuair in asthma have not been conducted". However, a lack of clinical studies of Duaklir Genuair in asthma, could not justify refusal of the application having regard to section II.C.7.2 and section II.C.5.3 of the EPO's Case Law of the Boards of Appeal, *supra*.

VI. The appellant requested that the decision under appeal be set aside and that the application be allowed on the basis of the main request refused by the examining division. Auxiliarily, the appellant requested that oral proceedings be appointed.

Reasons for the Decision

1. Claim 1 of the main request relates to a pharmaceutical composition comprising a pharmaceutically acceptable salt of aclidinium in the form of a dry powder with a dry powder carrier, which provides a metered nominal dose of aclidinium equivalent to 400 µg (plus/minus 10%) aclidinium bromide for use by inhalation in the treatment of asthma.

2. Sufficiency

2.1 Article 83 EPC requires that the application discloses the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

According to established jurisprudence of the Boards of Appeal of the EPO a convincing objection of lack of sufficiency of disclosure presupposes that there are serious doubts, substantiated by verifiable facts, on the possibility for a skilled person to carry out the invention as claimed. (see Case Law of the Boards of Appeal of the EPO, 9th Edition 2019, sections II.C. 7.1.4 and II.C.9; see also Guidelines for the Examination in the EPO, October 2019, F-III,1).

It is further established jurisprudence of the Boards of Appeal of the EPO that sufficiency of disclosure cannot be acknowledged, if an invention goes against a prevailing technical opinion and the patent fails to give even a single reproducible example (see Case Law of the Boards of Appeal of the EPO, *supra*, sections II.C.6.7 with reference to T 792/00, II.C.5.1 with reference to T 1164/11 and II.C.9 with reference to T 1273/09).

2.2 The application describes in paragraph [0002] under the heading "BACKGROUND" with reference to WO01/04118 that aclidinium bromide is a known long-acting anticholinergic agent with utility in the treatment of respiratory diseases, but that its optimal dose has not been disclosed. In the subsequent paragraph [0003] under the heading "SUMMARY OF THE INVENTION" the application states that it has been surprisingly found

that for treatment of respiratory disorders, in particular asthma and COPD, aclidinium is most effective upon administration by inhalation in a dosage of about 400 µg metered nominal dose. In the context of combinations with long-acting beta-2 agonists the application further refers to "the M3 antagonists of the invention" having a long duration of action (see paragraph [0032]) and thereby specifies the particular nature of the anticholinergic activity of aclidinium bromide. The application substantiates the effect of the defined dose of aclidinium in treatment of respiratory disease in Example 1 (paragraphs [0041]-[0044]). This example describes a trial in which patients with moderate to severe stable COPD received once daily treatment for 4 weeks with either aclidinium bromide (25, 50, 100, 200 or 400 µg), placebo or open-label tiotropium (18 µg) and wherein the aclidinium was well tolerated and at the higher doses achieved comparable bronchodilatory effects to tiotropium.

2.3 The decision under appeal suggests that on the basis of the information in the application and the common knowledge it was not plausible that aclidinium bromide was suitable for treatment of asthma. The application only presented experimental results concerning treatment of COPD, whereas it was part of the common knowledge as presented by document D5, that COPD and asthma are distinct diseases with different mechanisms involved.

Document D5 indeed mentions that the mechanisms of airway obstruction in COPD differ from that observed in asthma (see page 312, left-hand column, last paragraph) and that COPD is not associated with thickening of the lamina reticularis typical in asthma (see page 325, right-hand column, first paragraph final sentence).

Moreover, document D5 specifically states that anticholinergic drugs are potent bronchodilators in COPD, whereas the same beneficial effect is not observed in asthma, in which cholinergic mechanisms are of less importance (see page 327, left-hand column, second paragraph).

The Board observes, however, that document D5 thereby actually confirms, that asthma is influenced by cholinergic mechanisms, be it to a lesser extent than COPD, and that in asthma anticholinergic drugs do not show the same potency in beneficial bronchodilation as in COPD. The information in document D5 is therefore not considered to cast doubt on the statement in paragraph [0003] of the application that the defined dosing of aclidinium bromide is most effective for treating respiratory disorders, in particular asthma and COPD.

The Board thus considers the information in document D5 to be quite in line with the statement in paragraph [0002] of the application that aclidinium bromide was a long-acting anticholinergic agent with utility in the treatment of respiratory diseases as known for instance from WO01/04118. This statement finds further support in document D1, which mentions that M3 muscarinic receptor antagonists are useful in treatment of respiratory disorders such as asthma and COPD and describes aclidinium bromide as a M3 muscarinic receptor antagonist useful in combination with a PDE4 inhibitor in the treatment of such diseases (see D1: pages 9-10 bridging paragraph, page 1 lines 13-20 and page 22 lines 1-11). Moreover, document D3 describes anticholinergic agents, preferably tiotropium bromide, to act synergistically with corticosteroids in the treatment of inflammatory or obstructive respiratory

disorders such as asthma and COPD (see D3: page 1 lines 13-21, page 2 lines 6-9 and page 3 lines 17-26).

The Board does therefore not recognize that the claimed invention went against a prevailing technical opinion.

The decision under appeal further suggests that document D6 casts serious doubt on the defined utility of aclidinium bromide in asthma, because this document warns against using the product "Duaklir Genuair", which contains a relevant dose of aclidinimum bromide in combination with formoterol fumarate dihydrate, in treatment of asthma (see Decision, last paragraph of section 2.5).

The Board observes that the post-published document D6 relates to a summary of product characteristics from the Electronic Medicines Compendium (EMC), which contains information on licensed medicines for use in the UK. The warning in document D6 against the use of "Duaklir Genuair" in asthma is evidently related to the circumstance that no clinical studies regarding the use of "Duaklir Genuair" in treatment of asthma had been conducted. Accordingly, document D6 merely warns that the use of this combination product in asthma had not been officially authorized, which is *per se* not a ground for serious doubts regarding the claimed utility of aclidinium in treatment of asthma.

The Board therefore concludes that no serious doubts have come about, which would support the objection of lack of sufficient disclosure on which the decision under appeal is based.

2.4 Whilst the decision under appeal only briefly addresses the question of serious doubts regarding the defined

utility, the decision primarily relies for the finding of insufficient disclosure on the assessment that neither the application nor the prior art provided any evidence or disclosure that rendered effective treatment of asthma with aclidinium technically plausible. In this context the decision recalls that in case of a claim defining a specific therapeutic application the attaining of the claimed therapeutic effect is a functional technical feature of the claim and that as a consequence in line with the jurisprudence mentioned in the Case Law of the Boards of Appeal, *supra*, section II.C.7.2 the application must disclose the suitability of the product for the claimed therapeutic application.

2.5 The Boards of Appeal have indeed recognized that in the context of the requirement of sufficiency functional features require particular attention, as such features are defined by means of an effect that has to be achievable (see G 1/03, reasons 2.5.2). Occasional failure to achieve a defined effect does not necessarily imply insufficiency and reasonable experimentation by trial and error may be permissible, if the skilled person has adequate information, from the specification or on the basis of the common general knowledge, to achieve success in spite of initial failure (see Case Law of the Boards of Appeal, *supra*, section II.C.6.6.1, see also T 14/83, OJ 1984, 105, Headnote, and T 2220/14, reasons 63). Similarly, the definition of a group of compounds by both structural and functional features may be acceptable under Article 83 EPC, if the skilled person is able to identify without undue burden the compounds which fulfil the claimed functional requirements within the structurally defined group of compounds (see Case Law of the Boards of Appeal, *supra*, section II.C.6.6.9 with reference to

T 544/12). However, claims may not represent an invitation to perform a research programme without effective guidance towards success (see T 435/91, OJ 1995, 188, Headnote and Reasons 2.2.1). A crucial consideration in the assessment of the requirement of sufficiency in relation to functional definitions is the need for fair protection commensurate with the disclosed actual technical contribution (see T 1063/06, OJ 2009, 516, Headnote, T 694/92, OJ 1997, 408, Headnote and T 409/91, OJ 1994, 653, Headnote).

2.6 Section II.C.7.2 of the Case Law of the Boards of Appeal, *supra*, carries the heading "Level of disclosure required for medical use - plausibility". This section presents the considerations set out in T 609/02 and the jurisprudence that followed this decision.

In T 609/02 the competent board observed that, where a defined therapeutic effect is a functional technical feature of a claim, under Article 83 EPC, unless this is already known to the skilled person at the priority date, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application (see T 609/02, reasons 9). In line with the jurisprudence on functional definitions referred to in section 2.5 above, the reasons in T 609/02 recall the principle that the extent of a monopoly conferred by a patent should correspond to and be justified by the technical contribution to the art (see T 609/02, reasons 8). The claim in question covered limitless and untried downstream developments to yet to be demonstrated molecular mechanisms, which was considered to amount to no more than an invitation to set up further research programs for which no further guidance was forthcoming (see T 609/02, reasons 11). The competent board concluded that where at the

effective date no more than a vague indication of a possible medical use for a chemical compound yet to be identified is provided, later detailed evidence cannot be used to remedy the fundamental insufficiency of disclosure of such subject-matter (see T 609/02, reasons 13). In this context it was denied that a simple verbal statement regarding the utility of some compound X for a therapeutic purpose Y is enough to ensure sufficiency and that some information needs to be provided, for instance in the form of experimental tests, to the avail that the defined agent has a relevant effect (see T 609/02, reasons 9). Notably, neither T 609/02 nor the jurisprudence that developed from this decision signal a deviation from the established jurisprudence or an interpretation differing from the Guidelines, in particular with respect to the precondition of serious doubts for a convincing argument of lack of sufficiency.

2.7 As explained in section 2.3 above the Board takes the view that in the present case the defined utility of aclidinium in treatment of asthma does not go against any prevailing opinion in the prior art. In this context the Board considers the statement in the application, that the treatment of respiratory disorders, particularly asthma and COPD, with aclidinium is most effective upon administration by inhalation in a dosage of about 400 µg metered nominal dose (paragraph [0003]) to represent a significant technical teaching, which is far from an invitation to perform a research programme and which does not *prima facie* lack plausibility. This teaching is as such falsifiable, in the sense that it is open to challenge, and is therefore considered to represent information in the form of a specific technical contribution which goes beyond some insufficient verbal statement. In line

with the established jurisprudence as discussed in sections 2.5 and 2.6 above the sufficiency of the disclosure of the claimed invention is therefore not to be denied following the Board's assessment as set out in section 2.3 above, that no serious doubts have come about with respect to the defined utility.

2.8 Accordingly, the Board is of the opinion that the claimed invention is sufficiently disclosed.

3. Inventive step

3.1 In its communication of 27 February 2017 the examining division raised an objection of lack of inventive step against the claimed subject-matter based on the teaching in document D1 as closest prior art, which already described the utility of aclidinium bromide in treatment of asthma. This objection was subsequently replaced by the examining division's objection of lack of sufficient disclosure on which the decision under appeal was based.

In view of this development during the examination procedure and having regard to the applicant's request, that the application be allowed on the basis of the main request, the Board does not see any special reasons for remitting the case to the examining division for further prosecution. Instead the Board presents the following assessment regarding the inventive merit of the claimed invention with respect to the cited prior art.

3.2 The assessment of inventive step based on the problem-solution-approach involves the initial identification of the differences between the claimed subject-matter and the closest prior art, which is followed by the

formulation of the problem to be solved in the light of these differences and their technical effects. The question to be answered is whether, at the relevant date, the skilled person would on the basis of the available prior art have arrived at the claimed matter as a solution to the relevant problem in an obvious manner. In the formulation of the relevant problem care has to be taken that the relevant problem and its claimed solution may indeed be plausibly derived from the application as originally filed (see Case Law of the Boards of Appeal, *supra*, section I.D.4.6 with reference to T 1329/04 and T 488/16, see also T 1677/11, reasons 9.5.1) and that on the basis of all available information the claimed subject-matter may indeed be considered to credibly solve such problem (see T 939/92, OJ 1996, 309, reasons 2.6,). Considerations derived from the prior art for accepting that a problem is solved also apply in assessing obviousness (see T 964/92, reasons 2.8 and T 532/06, reasons 3.1.3).

3.3 Document D1 describes the combination of a M3 muscarinic receptor antagonist such as aclidinium bromide with a PDE4 inhibitor, preferably in the form of compositions for inhalation, to be useful in treatment of respiratory disorders such as asthma and COPD (see page 1 lines 13-20, pages 9-10 bridging paragraph, page 22 lines 1-11, page 33 lines 2-4). The document mentions for the M3 muscarinic receptor antagonist a suitable dosage unit of 20-1000 µg, preferably 50-300 µg (see page 32, 10-13) and describes in its examples 1-2 formulations comprising 100 µg aclidinium bromide (see page 33). The document mentions that the defined combination provides for an unexpected beneficial therapeutic effect allowing the use of smaller doses than would be the case with the

individual agents used in monotherapy and thereby reducing the side effects that may occur when the agents are administered alone (see page 2 lines 6-13 and page 34 under "Pharmacological activity").

The Board finds no evidence on file that this teaching in document D1 went against a prevailing opinion at the time of its disclosure. Moreover, no serious doubts have arisen that would otherwise compromise the information from document D1. The Board therefore agrees with the mentioned initial assessment by the examining division that document D1 represents a suitable starting point in the prior art for the assessment of inventive step.

3.4 The difference between the subject-matter of claim 1 of the main request and the teaching in document D1 concerns the definition of the particular metered nominal dose of aclidinium equivalent to 400 µg (plus/ minus 10%) aclidinium bromide.

The application states in paragraph [0003] that it has been surprisingly found that for treatment of respiratory disorders, in particular asthma and COPD, aclidinium is most effective upon administration by inhalation in a dosage of about 400 µg metered nominal dose. The Board takes the view that this statement is corroborated by the results of the trial of Example 1 of the application(paragraphs [0041]-[0044]). In this trial patients with moderate to severe stable COPD received once daily treatment for 4 weeks with either aclidinium bromide(25, 50, 100, 200 or 400 µg), placebo or open-label tiotropium (18 µg). Unlike tiotriopium, aclidinium is reported to induce a comparable bronchodilatory effect during the first 6 hours post-dose on day 29 and day 1. The aclidinium was well

tolerated, with no dose-dependent effect on ECG, laboratory parameters or adverse events. Aclidinium 200 and 400 µg had comparable bronchodilatory effects to open-label tiotropium 18 µg. The application states that based on the efficacy and tolerability data, aclidinium 400 µg is selected as the investigational dose for a future long-term clinical trial in COPD.

In the light of this disclosure the Board is satisfied that the problem of providing an optimized dose with respect to efficacy and side effects for treatment of asthma with aclidinium and its claimed solution may be plausibly derived from the application as filed.

The post-published document D4 describes a further trial involving the treatment of patients with COPD by twice daily administration of a 100, 200 or 400 µg dose of aclidinium bromide during 7 consecutive days. The greatest improvements in lung function and reduction of required further daily relief medication were observed with the 400 µg dose, which was not found to be associated with an increase in side effects (see section "Results" on pages 250-251 and page 252 final paragraph).

On the basis of the information from document D1 that aclidinium bromide was known as a M3 muscarinic receptor antagonist with utility in treatment of respiratory disorders such as asthma and COPD and the confirmation in document D5 that asthma is influenced by cholinergic mechanisms, be it to a lesser extent than COPD (see item 2.3 above), the Board takes the view that it is reasonable to assume that the optimized dose for relief of patients suffering from COPD also represents an optimized dose for relief of patients suffering from asthma. In fact, the trial reported in

the application as well as the study of document D4 investigate the bronchodilatory effects of different doses of aclidinium. Asthma and COPD are both obstructive disorders of the respiratory tract (see document D3, page 3, lines 17-21). It may therefore be assumed that bronchodilation is beneficial in both conditions and that the dose-related effects observed in COPD patients are likely to be present also in asthma patients.

The Board therefore concludes that having regard to the results reported in Example 1 of the application and the results reported in document D4 the problem of providing an optimized dose with respect to efficacy and side effects for treatment of asthma may indeed be considered credibly solved by application of the defined 400 µg dose.

3.5 The Board finds no information in the available prior art in view of which the skilled person would as a matter of obviousness arrive at the claimed subject-matter as solution to the problem identified in section 3.4 above.

Document D1 itself mentions 20-1000 µg as suitable dosage unit for the M3 muscarinic receptor antagonist to be used, but describes a dosage unit of 50-300 µg as preferred (see page 10-13). The presented examples of formulations comprising aclidinium only contain a 100 µg dose of aclidinium bromide (see examples 1-2). Moreover, the teaching of document D1 was actually aimed at lowering the dosing of the individual agents by use of a combination of agents in order to reduce unwanted side effects such as may occur when the agents are administered alone (see page 2 lines 6-13).

Accordingly, document D1 does not provide any suggestion towards an optimized dose of 400 µg

Document D2 presents a short summary of a trial in which patients suffering form COPD were administered a single dose of 100, 300 or 900 µg of aclidinium bromide. The 300 and 900 µg dose produced similar peak FEV_1 effects and these effects were greater and earlier than the effect of the lowest dose. All single doses of aclidinium were reported to be well tolerated and effective in producing long-lasting (>24 hours) bronchodilation. As explained in section 3.4 above, the Board acknowledges that it is not unreasonable to assume that an optimized dose for relief of patients suffering from COPD also represents an optimized dose for relief of patients suffering from asthma (see section 3.4 above). However, document D2 concerns a single dose study, whereas asthma is well known to be a chronic disease. Moreover, the similar effects from the 300 and 900 µg dose reported in document D2 suggest that an optimum effect could already be achieved at a dose of 300 µg or even lower. The Board therefore takes the view that the results from the single dose trial of document D2 actually seem to teach away from an optimized dose of 400 µg for treatment of a chronic disease such as asthma.

Having regard to the prior art as represented by documents D1 and D2 the Board is of the opinion that the defined subject-matter of claim 1 is not the obvious result of routine experimentation, but rather represents the unexpected outcome of a study for finding an aclidinium dose for treatment of a chronic disease which combines optimized effectiveness with the absence of side effects.

3.6 Accordingly, the Board concludes that the subject-matter of claim 1 involves an inventive step.

4. Independent claim 11 relates to aclidinium in free or pharmaceutically acceptable salt form for use in treating asthma in a patient in need of such treatment, wherein the use comprises administration by inhalation once or twice daily of a metered nominal dose of aclidinium equivalent to 400 µg (plus/minus 10%) aclidinium bromide. Independent claim 16 defines the same utility in the so-called "Swiss-type" format.

These claims thus also relate to the utility of the optimized dose of 400 µg aclidinium in treatment of asthma by inhalation. The Board therefore takes the view that the same observations as set out above with respect to claim 1 apply to claims 11 and 16.

The examining division raised no further objections with respect to claims 11 or 16 or any of the dependent claims. The Board finds no grounds for further objections either.

5. The Board is aware of concerns, that patents in the field of medicine should not be granted on the basis of pure speculation.

The Board observes in this context that claims in patent applications typically involve generalisations which inherently include an aspect of speculation. Patent applications in the field of medicine represent in this respect no exception. As explained in sections 2.1-2.6 and 3.2 above, the approaches developed in the jurisprudence of the Boards of Appeal of the EPO for the assessment of sufficiency of disclosure and inventive step specifically take account of the

technical contribution actually disclosed in a patent application to avoid patent protection resulting from unreasonable speculation on the basis of propositions that are *prima facie* implausible.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Examining Division with the order to grant a patent on the basis of claims 1-17 of the main request filed on 17 December 2018 and a description to be adapted thereto.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated