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Case Number: T 0609/12 - 3.3.01

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Language of the proceedings: EN

Title of invention:
COMBINATION OF AZELASTINE AND FLUTICASONE

Patent Proprietor:
Cipla Limited

Opponent:
Glaxo Group Limited

Headword:
Azelastine with fluticasone ester/CIPLA

Relevant legal provisions:
EPC Art. 114(2), 56, 111(1)
RPBA Art. 12(2), 12(4), 13(1)

Keyword:
Late-filed evidence
Inventive step - improvement not shown, reformulation of the technical problem
Remittal to the department of first instance for examination of auxiliary requests - no
Late-filed requests submitted during oral proceedings - admitted (no)

Decisions cited:

Catchword:

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Case Number: T 0609/12 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 31 May 2017

Appellant: (Opponent)	Glaxo Group Limited Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN (GB)
Representative:	Goddard, Carolyn Janice GlaxoSmithKline Global Patents (CN925.1) 980 Great West Road Brentford, Middlesex TW8 9GS (GB)
Respondent: (Patent Proprietor)	Cipla Limited Cipla House Peninsula Business Park Ganpatrao Kadam Marg Lower Parel Mumbai - 400013 (IN)
Representative:	Turner, Craig Robert A.A. Thornton & Co. 10 Old Bailey London EC4M 7NG (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 19 January 2012 concerning maintenance of the European Patent No. 1519731 in amended form.**

Composition of the Board:

Chairman	L. Bühler
Members:	J. Molina de Alba
	M. Pregetter

Summary of Facts and Submissions

I. The present appeal lies from the decision of the opposition division concerning maintenance of European patent No. 1 519 731 in amended form on the basis of auxiliary request 1 filed with letter of 11 August 2011, with the following claim 1:

"1. A pharmaceutical formulation which comprises azelastine, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable ester of fluticasone, wherein the pharmaceutical formulation is in a form suitable for nasal or ocular administration."

II. The following documents, cited during the opposition/ appeal proceedings, are referred to below:

(1) EP-A-0 780 127

(2) Dykewicz et al., Ann. Allergy Asthma Immunol., 1998, 81, 478-518

(3) ABPI Data Sheet for Flixonase Aqueous Nasal Spray, 1999-2000

(11) Johnson M., J. Allergy Clin. Immunol., 1998, 101(4) Part 2, S434-S439

(21) Ms Malhotra's declaration of 11 August 2011

(22) Malhotra Exhibit A

(23) Malhotra Exhibit B

(24) Dr Maus' declaration of 17 August 2011

(25) Maus Exhibit B

(26) Maus Exhibit C - Juniper E.F. et al., J. Allergy Clin. Immunol., 1989, 83(3), 627-633

(27) Maus Exhibit D - Ratner, P.H. et al., J. Fam. Pract., 1998, 47(2), 118-125

(28) Maus Exhibit E - Simpson R.J., Ann. Allergy, 1994, 73(6), 497-502

(29) Maus Exhibit F - Howarth P.H., Allergy, 2000, 62, 6-11

(30) Maus Exhibit G - Nielsen L.P. et al., Drugs, 2001, 61(11), 1563-1579

(31) Maux Exhibit H - Salib R.J. et al., Drug Safety, 2003, 26(12), 863-893

(32) Hampel, F.C. et al., Ann. Allergy Asthma Immunol., 2010, 105, 168-173

(47) Waddell, A.N. et al., J. Laryngol. Otol., 2003, 117(11), 843-845

(48) Wilson, A.M. et al., J. Allergy Clin. Immunol., 1998, 101(4) Part 1, 470-474

(49) Blaiss, M.S., Allergy and Asthma Proc., 2001, 22(6) Suppl. 1, S5-S10

(50) Mandl, M. et al., Ann. Allergy Asthma Immunol., 1997, 79, 370-378

(51) Malone D. et al., J. Allergy Clin. Immunol., 2000, Abstracts, S390

III. In the decision under appeal, the opposition division did not admit into the proceedings *inter alia* documents (11) and (26) to (31) but admitted documents (21) to (25) and (32). It further admitted auxiliary request 1 and considered that the claims of that request fulfilled the requirements of the EPC.

In its analysis of inventive step, the opposition division identified example III of document (1) as the closest prior art and defined the technical problem underlying the invention as the provision of a pharmaceutical formulation comprising azelastine and a glucocorticosteroid having improved properties for use in the treatment of allergic rhinitis (see point 13.3.4 of the appealed decision). Based on the comparative stability data provided in documents (22) and (23) and the clinical tests presented in documents (24), (25) and (32), the division acknowledged that the solution proposed in claim 1, namely the replacement of the glucocorticosteroid triamcinolone acetonide in the closest prior art by a fluticasone ester, solved the problem posed in a non-obvious manner.

IV. The opponent (appellant) filed notice of appeal against this decision. With its statement of grounds of appeal, it requested that the decision be set aside and that the patent be revoked because the version held allowable by the opposition division contravened Articles 123(2), 83, 54 and 56 EPC. In addition, the appellant requested that *inter alia* document (11) be admitted into the appeal proceedings.

V. In its reply to the statement of grounds of appeal, the patent proprietor (respondent) requested that the appeal be dismissed or, alternatively, that the patent be maintained on the basis of any of the four auxiliary requests filed therewith. In addition, the respondent requested that *inter alia* documents (26) to (31) be admitted into the proceedings.

Claim 1 of auxiliary request 1 differs from claim 1 of the main request (i.e. the request forming the basis for the appealed decision, see point I above) in the specification that the ester of fluticasone is "in an amount from 50 micrograms/ml to 5 mg/ml of the formulation".

Claim 1 of auxiliary request 2 differs from claim 1 of the main request in the selection of fluticasone propionate as the ester of fluticasone.

Claim 1 of auxiliary request 3 results from the combination of the limitations in claim 1 of auxiliary requests 1 and 2.

Claim 1 of auxiliary request 4 differs from claim 1 of auxiliary request 3 in the specification that azelastine is present as azelastine hydrochloride.

VI. In a communication sent as annex to the summons to oral proceedings, the board was of the preliminary opinion that the opposition division's decision not to admit documents (11) and (26) to (31) should be reversed. By contrast, it concurred with the division that the claims of the main request met the requirements of Articles 123(2), 83 and 54 EPC.

VII. In response to the board's preliminary opinion, the respondent requested the admission of documents (47) to (51) in the event that document (11) were to be admitted into the proceedings.

VIII. Oral proceedings were held before the board on 31 May 2017. The appellant was absent, as previously announced with letter of 19 May 2017.

In the course of oral proceedings, the respondent filed a request for remittal of the case to the opposition division if the appeal were not dismissed. In addition, it filed auxiliary requests 5 and 6.

Claim 1 of auxiliary request 5 was based on claim 1 of the main request, from which ocular administration had been removed and where the additional ingredients microcrystalline cellulose and carboxy methyl cellulose sodium had been added.

Claim 1 of auxiliary request 6 was based on claim 1 of auxiliary request 5, with the insertion of the additional ingredient phenyl ethyl alcohol.

IX. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

With regard to the admission of document (11), the appellant submitted (see pages 3-4 of the statement of grounds of appeal) that the reason given by the opposition division not to admit the document, namely that it was *prima facie* not closer to the invention than other documents on file, was flawed. In the appellant's view, the document should have been admitted because it had been filed in reaction to the patentee's response to the statement of grounds of

opposition and because it *prima facie* prejudiced the maintenance of the patent, since it showed that the skilled person had a clear motivation to select fluticasone propionate as replacement for triamcinolone acetonide in the closest prior art.

The appellant did not object to the admission of documents (26) to (31) and (47) to (51).

In its analysis of inventive step of the main request, the appellant identified two alternative disclosures within document (1) that represented the most promising starting points (see statement of grounds of appeal: page 21, paragraph 3 and point 6.8): either the combination of example III with the passage on page 6, lines 44-46, which taught a formulation for intranasal administration comprising fluticasone and azelastine hydrochloride; or example III in isolation, which taught a formulation comprising triamcinolone acetonide and azelastine hydrochloride. In both cases, the invention differed from the closest prior art in that the corticosteroid combined with azelastine was a fluticasone ester.

Contrary to the opposition division's opinion, the appellant held that the problem to be solved could not be formulated as an improvement because the comparative data presented by the respondent in documents (22) to (25) did not provide an appropriate comparison with the closest prior art (see statement of grounds of appeal: point 6.4, paragraphs 1 and 2; page 17, last paragraph; and point 6.5, paragraph 1). Hence, depending on the closest prior art selected, the problem to be solved had to be formulated either as the provision of a combination of azelastine hydrochloride and an alternative form of fluticasone, or as the provision of

further combinations of azelastine hydrochloride and a glucocorticosteriod (see statement of grounds of appeal, last sentence before point 6.7 and point 6.8, respectively).

The solution to the first problem was obvious because at the filing date the only form of fluticasone commercially available for the treatment of allergic rhinitis was the ester fluticasone propionate (see document (3)). The solution to the second problem was likewise obvious because document (11) suggested the superior pharmacological properties of fluticasone propionate over other glucocorticosteroids, including those disclosed in document (1).

The appellant did not take position with regard to the auxiliary requests.

X. The respondent's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

On the admission of document (11), the respondent argued (see letter of 28 April 2017, page 2, paragraphs 4-5) that it was not *prima facie* relevant to the assessment of inventive step because it related to the treatment of asthma and lung uptake and its observations that fluticasone propionate exhibited higher *in vitro* potency and lipophilicity were not necessarily positive features for the treatment of nasal or ocular symptoms. In fact, higher potency was associated with greater undesirable side-effects, and higher lipophilicity made co-formulation with azelastine more difficult.

Turning to the admission of documents (26) to (31), the respondent submitted that they were an integral part of the declaration of Dr Maus (document (24)), which had been admitted by the opposition division. In addition, the documents were highly relevant to the assessment of inventive step because documents (26) to (29) taught that antihistamine/glucocorticosteroid combinations other than those claimed in the patent in suit did not show any improved clinical response, and documents (30) and (31) addressed the appellant's contention that fluticasone propionate was the steroid of choice at the filing date.

With respect to the admission of documents (47) to (51), the respondent explained that they had been filed in reaction to the preliminary opinion of the board, which considered document (11) to be highly relevant and intended to admit it into the proceedings. Thus, documents (47) to (51) were intended to counter a danger of misrepresentation of the prior art if document (11) were taken in isolation, since documents (47) to (51) depicted the general knowledge at the filing date that fluticasone propionate was not the steroid of choice for the treatment of allergic rhinitis.

In its analysis of inventive step of the main request, the respondent argued that the selection of a specific example as the closest prior art could be made only with hindsight (see response to the statement of grounds of appeal, point 7.9.1) and that the closest prior art was rather represented by the teaching of document (1) as a whole, i.e. the combination of an antihistamine and a glucocorticosteroid for the treatment of allergic rhinitis by nasal administration. Nevertheless, in reaction to the board's opinion in

this respect during oral proceedings, the respondent provided additional arguments starting from example III of document (1) as the closest prior art.

On the basis of the disclosure in paragraph [0006] of the patent in suit, the respondent defined the problem to be solved as the preparation of a formulation comprising azelastine and a glucocorticosteroid with **improved stability and improved effectiveness** for the treatment of allergic rhinitis.

Having regard to the experimental evidence provided in documents (22) and (25), the respondent considered that the formulation proposed in claim 1 solved the problem posed, and that it did so in a non-obvious manner because the prior art contained no hint to combine azelastine with a fluticasone ester in the expectation of improving the stability and efficacy of the formulation of example III of document (1).

In response to the board's concerns that the tests in document (22) would not be suitable to demonstrate a stability improvement due to the different nature and amount of some excipients in the formulations of columns 1 and 3, the respondent submitted that said differences were minor and that the excipients tested were equivalent. Moreover, given the low concentrations of the excipients they could not be expected to have a substantial influence on the stability of the composition. Thus, the difference in stability between the claimed formulation (column 1) and that of example III (column 3) had to be ascribed to their respective active compounds.

The respondent likewise provided arguments addressing the eventuality that the technical problem had to be

reformulated in a less ambitious way, i.e. as an **alternative**, if the board came to the conclusion that the evidence on file did not show an improvement.

For such a case, the respondent maintained that the solution proposed in claim 1 would remain inventive because the teaching of documents (47) to (51) would have dissuaded the skilled person from choosing a fluticasone ester as the intranasal steroid to replace triamcinolone acetonide in example III of document (1), for at least four reasons: firstly, because said documents concluded that fluticasone propionate was not more effective than other intranasal steroids for the treatment of allergic rhinitis (see document (47): abstract, point 2; document (49): page S6, column 1, paragraphs 1-3; document (50): page 374, column 3; and document (51): abstract); secondly, because fluticasone propionate presented important side-effects over other intranasal steroids (see document (47): abstract, point 2; and page 844, column 2, paragraph 1; document (48): conclusion in the abstract; page 470, column 2, paragraph 2; and page 473, column 1, paragraphs 2-3); thirdly, because patients preferred triamcinolone acetonide over fluticasone propionate (see document (49): figures 1 and 3); and, fourthly, because medical care costs of the treatment with fluticasone were higher than with triamcinolone acetonide (see document (51): abstract).

Finally, in response to the appellant's argument that fluticasone propionate was the steroid of choice in view of its allegedly superior pharmacological properties disclosed in document (11), the respondent stressed that this document showed *in vitro* studies and therefore their results did not equate to an increased *in vivo* efficacy, as was apparent from documents (47)

to (51). In addition, the higher lipophilicity and vasoconstrictor activity of fluticasone propionate disclosed in document (11) raised concerns over its safety, on the one hand because a higher lipophilicity was linked to a greater systemic availability and, consequently, to greater side-effects (see document (48): page 473, column 1, paragraphs 2-3) and on the other hand because a greater vasoconstrictor activity increased the risk of nasal septal perforation (see document (31): abstract, paragraph 2; and page 877, column 1, paragraph 2). Hence, document (11) discouraged the skilled person from using fluticasone propionate as an intranasal steroid.

As to its request for remittal of the case to the opposition division for consideration of the auxiliary requests, the respondent explained that this would give it the opportunity to have its auxiliary requests examined by two instances and to correct the deficiencies in the experimental data pointed out by the board during oral proceedings. Such corrections had not been necessary before because the opposition division considered the present main request to be inventive.

With respect to the inventive step of auxiliary request 1, the respondent noted that, in addition to the arguments presented for the main request, the limitation in the amount of fluticasone ester introduced in claim 1 was not specifically taught in document (1) and was therefore not obvious.

Similar submissions were made in relation to auxiliary requests 2 to 4. In addition, the respondent stated that the additional limitations made the stability and efficacy improvements shown more credible.

Regarding the admission of auxiliary request 5, the respondent submitted that it had been filed in response to the board's objections to the comparative tests in document (22), raised during oral proceedings. Thus, the thickener used in said tests in the formulation according to the invention, i.e. a combination of microcrystalline cellulose and carboxy methyl cellulose sodium, had been introduced into claim 1 based on its disclosure as Avicel RC 591 or Avicel CL11 in the application as filed (see page 4, paragraph 3 from the bottom, and examples 3 to 5). In addition, the respondent noted that, although the new feature had been taken from the description, it was easy to consider and could not take the appellant by surprise because the issue of the different excipients in the comparative tests of document (22) had been raised in the statement of grounds of appeal.

On the admission of auxiliary request 6, the respondent indicated that, in addition to the reasons presented for auxiliary request 5, the introduction of the feature "phenyl ethyl alcohol" represented a further limitation based on the examples of the application as filed. This amendment would also render the formulation of claim 1 inventive because phenyl ethyl alcohol was not present in example III of document (1).

XI. In the written procedure, the appellant had requested that the decision under appeal be set aside and that the patent be revoked.

XII. The respondent's final requests, as confirmed at the end of the oral proceedings before the board, were that the appeal be dismissed (main request), or alternatively that the case be remitted to the

opposition division for further prosecution, or alternatively that the patent be maintained in amended form on the basis of any of auxiliary requests 1 to 4, filed with the reply to the statement of grounds of appeal, or auxiliary request 5 or 6, filed the during oral proceedings before the board.

XIII. At the end of the proceedings, the board's decision was announced.

Reasons for the Decision

1. The appeal is admissible.

2. Admission of documents (11) and (26) to (31) into the appeal proceedings - Article 114(2) EPC and Article 12(4) RPBA

2.1 The opposition division did not admit document (11) into the proceedings because, in its opinion, it appeared not to be prima facie more relevant to inventive step than documents (1) and (2), which were already on file and were considered "pertinent starting points" (see point 2.2.3 of the decision).

Contrary to the opposition division's opinion, a newly filed document does not have to be more relevant than the closest prior art in order to become relevant to a ground for opposition under consideration. In the present case, document (11) was filed by the opponent to support its inventive step argument that, at the filing date, fluticasone propionate was the corticosteroid of choice for replacing triamcinolone acetonide in example III of document (1), which was considered to be the closest prior art (see letter of 8 August 2011, point 8.1.4). As document (11) discloses

what could be seen as superior properties of fluticasone propionate compared to triamcinolone acetonide, it is *prima facie* highly relevant to the issue of obviousness. In addition, the document was filed in response to the opposition division's preliminary opinion, and the respondent had more than two months to react before oral proceedings. Hence, the board has concluded that the opposition division did not properly exercise its discretion with regard to document (11) and has decided to overturn its decision not to admit the document into the proceedings.

2.2 Documents (26) to (31) were filed two months before oral proceedings before the opposition division as integral parts of the declaration of Dr Maus (document (24)), which was admitted into the opposition proceedings. With these documents, the patentee intended to depict the general knowledge of the skilled person at the priority date that the combination of an oral antihistamine with an intranasal corticosteroid provided no or minimal additional clinical effect in the treatment of allergic rhinitis compared to the therapy with an intranasal steroid alone (see document (24), points 15 to 19).

Document (30) is a review of the use of intranasal corticosteroids for treating allergic rhinitis published shortly before the priority date of the patent in suit. In its point 3.3, the document refers to four studies on the combination of antihistamines with intranasal corticosteroids, three of which, corresponding to documents (26) to (28), did not show any benefit over the treatment with the corticosteroid alone. In addition, document (29) mentions the limited studies available in this respect (see passage bridging pages 9 and 10).

Document (31) is a review article published shortly after the priority date of the patent in suit and refers back to documents (29) and (30) (see page 886 and references 112 and 126), published before said date. Thus, document (31) could be considered for assessing the skilled person's knowledge at the priority date. The document concludes that there is no evidence that combination therapy provides an additional benefit over monotherapy with corticosteroids.

In conclusion, documents (26) to (31) support the argument for which they were filed and are *prima facie* relevant to the discussion of inventive step. The opposition division's decision not to admit these documents into the proceedings, substantiated merely by a statement that the documents did not appear to be *prima facie* relevant for inventive step (see decision, point 2.3.2, last sentence), has been reversed by the board.

3. *Admission of documents (47) to (51) - Article 114(2) EPC and Article 13(1) RPBA*

Documents (47) to (51) were filed during the appeal proceedings in reaction to the board's preliminary opinion that the opposition division's decision not to admit document (11) should be reversed. The documents were filed by the respondent to show that, contrary to what might be derived from reading document (11) in isolation, the general knowledge at the filing date was that fluticasone propionate was not the steroid of choice for the treatment of allergic rhinitis. In this context, the board notes that, similarly to document (31) (see point 3.2), document (47) is a review article

published shortly after the priority date and that the relevant documents to which it refers were published before that date. Therefore, document (47) could also be taken into account for assessing the skilled person's knowledge at the priority date.

Considering that the documents were filed in reaction to the board's preliminary opinion more than one month before oral proceedings, that they could be quickly analysed and that they effectively supported the argument that fluticasone propionate was not the preferred corticosteroid for the treatment of allergic rhinitis at the priority date (see document (47): abstract, point 2 and page 844, column 1, paragraph 2; document (48): abstract and page 473, column 1, paragraphs 2-3; document (49): page S6, column 1, paragraphs 1-3, and figures 1-3; document (50): page 374, column 3, paragraph 1; and document (51): abstract 1138), the board has decided to admit them into the appeal proceedings.

4. Main request - inventive step - Article 56 EPC

4.1 Closest prior art

Both parties and the opposition division proposed document (1) as the closest prior art because it was concerned with the use of combinations of an antihistamine and a corticosteroid for the treatment of allergic rhinitis by intranasal administration. Within the teaching of document (1), however, three alternative starting points were proposed:

- The appellant's first choice was the combination of example III with the passage on page 6, lines 44-46, which teaches the treatment of allergic rhinitis by

intranasal administration of a formulation comprising fluticasone and azelastine.

- The appellant's second choice, in line with the opposition division's opinion, was example III as such, which teaches the treatment of allergic rhinitis by intranasal administration of a formulation comprising triamcinolone acetonide and azelastine.

- Finally, the respondent's choice was the teaching of document (1) as a whole, i.e. the treatment of allergic rhinitis by intranasal administration of a formulation comprising an antihistamine and a corticosteroid.

In the board's view, the combination of passages taken by the appellant as its first choice is not an unambiguous disclosure of the combination of fluticasone and azelastine but rather a suggestion thereof. Thus, said passage combination is not a suitable starting point for the problem-solution approach. Regarding the two other choices, the board considers example III to be closer to the invention than the general teaching of document (1), because the former differs from the formulation of claim 1 only in the corticosteroid while the latter differs in the choice of both corticosteroid and antihistamine. Consequently, the board concurs with the appellant and the opposition division that example III of document (1) represents the closest prior art.

In this respect, the respondent's argument that the choice of a specific embodiment within the disclosure of document (1) could only be made with hindsight has not convinced the board, on the one hand because the choice of the closest prior art necessarily requires the knowledge of the invention and on the other hand

because Article 56 EPC requires that an invention be non-obvious with regard to the prior art, i.e. with regard to every piece of prior art. Hence, the choice of a specific embodiment as the most promising starting point is appropriate.

4.2 Problem to be solved

The formulation of claim 1 differs from that in example III of document (1) in the corticosteroid, which is a fluticasone ester instead of triamcinolone acetonide.

Based on this difference, the respondent formulated the technical problem underlying the invention as the provision of a formulation comprising azelastine and a glucocorticosteroid with improved stability and improved effectiveness in the treatment of allergic rhinitis. In addition, the respondent held that the comparative tests provided in documents (22) and (25) proved that the problem had been effectively solved by the formulation proposed in claim 1.

On the latter point, however, the board agrees with the appellant's position that documents (22) and (25) fail to show any stability or therapeutic improvement over the closest prior art because they do not provide an appropriate comparison with example III of document (1):

In document (22), the formulation according to the invention (column 1) differs from that of example III of document (22) (column 3) not only in the corticosteroid but also in the nature and amount of the excipients, in particular the nature and amount of the thickening agent (Avicel RC 591 at 1.5% vs HPMC at 1.0%) and the amount of surfactant (Polysorbate 80 at

0.025% vs 0.05%). Thus, the higher stability of the formulation in column 1 cannot be exclusively ascribed to the different corticosteroid. This was countered by the respondent at the oral proceedings before the board with the argument that the excipients in the examples of document (22) were equivalent and that they were present in such low concentrations that they could not be expected to cause any difference in the stability of the formulations. This argument, however, did not convince the board because ionic and non-ionic thickeners cannot be regarded as being equivalent and because their concentrations, albeit low, correspond to their customary values. In addition, the fact that the amounts of thickener and surfactant differed from one formulation to the other in a relationship of 50 to 100% could not be neglected either.

Similarly, document (25) does not provide any comparison between the therapeutic effect produced by the combination of azelastine/fluticasone ester and that of azelastine/triamcinolone acetonide. Thus, the tests in document (25) are likewise unsuitable to show any improvement over the closest prior art. In this context, the respondent's argument that, contrary to the skilled person's expectations, the combination therapy with azelastine and fluticasone ester produces a higher therapeutic effect than the monotherapy with azelastine or fluticasone ester cannot be taken into account.

4.3 Reformulation of the problem to be solved

In view of the lack of evidence proving that the above-formulated problem is solved by the solution proposed in claim 1, the problem needs to be reformulated in a less ambitious way, namely as the provision of a

further formulation comprising azelastine and a glucocorticosteroid for the treatment of allergic rhinitis.

The board is convinced that this problem is effectively solved by the formulation of claim 1 because both azelastine and fluticasone esters are known therapeutic agents for treating allergic rhinitis by intranasal administration (see e.g. documents (1) and (3)).

4.4 Obviousness

At the filing date, a particular fluticasone ester, namely fluticasone propionate, was one of the standard intranasal corticosteroids for the treatment of allergic rhinitis (see document (3): page 43, column 2; and document (27): page 118, column 2, paragraph 2) and, in that context, it was regarded as equivalent to triamcinolone acetonide (see document (47): abstract, point 2; page 844, column 1, paragraph 2; and document (49): page S6, column 1, paragraphs 2-3). Accordingly, the skilled person searching for further formulations comprising azelastine and a glucocorticosteroid for the treatment of allergic rhinitis would have replaced triamcinolone acetonide with fluticasone propionate in example III of document (1) as one of the obvious solutions to the problem posed. Thereby he would have arrived at the formulation of claim 1 without the involvement of an inventive step.

The respondent replied that the skilled person would have been deterred from using fluticasone propionate instead of triamcinolone acetonide because the former had more important secondary effects and was less preferred by patients, as derived from the studies in documents (47) to (49) and (51). Thus, documents (47)

and (48) (see document (47): abstract, point 4 and page 844, column 2, paragraph 1; document (48): conclusion in the abstract and page 473, column 1, paragraphs 2-3) showed that fluticasone caused a significantly higher reduction of overnight urinary cortisol secretion than triamcinolone acetonide, while document (49) (see figures 1-3 and page S9) disclosed the higher preference of patients for triamcinolone acetonide over fluticasone propionate, and the study in document (51) found that the overall costs for treating allergic rhinitis with triamcinolone acetonide were significantly lower compared to fluticasone propionate. In addition, the higher lipophilicity and vasoconstrictor activity of fluticasone propionate observed in document (11) (see abstract and table III) would have raised safety concerns because higher lipophilicity was linked to greater systemic availability and, consequently, to greater side-effects (see document (48): page 473, column 1, paragraphs 2-3), and greater vasoconstrictor activity increased the risk of nasal septal perforation (see document (31): abstract, paragraph 2; and page 877, column 1, paragraph 2).

The board cannot accept these arguments, firstly because the problem to be solved has been defined in terms of the formulation's therapeutic effect without consideration of secondary effects that, in the absence of proof of the contrary, would still be present in the formulation of claim 1, and secondly because fluticasone propionate was considered to be safe at the filing date since it was marketed as a nasal spray for the treatment of allergic rhinitis (see document (3)). As a result, the respondent's argument that the skilled person would be deterred from using fluticasone propionate as an alternative to triamcinolone acetonide

has to be dismissed, and the subject-matter of claim 1 of the main request lacks inventive step.

5. *Remittal - Article 111(1) EPC*

The respondent requested that, in the event that the board did not allow the main request, the case be remitted to the opposition division for further prosecution on the basis of the auxiliary requests in order to have the latter examined by two instances and to have the opportunity to correct the deficiencies in data pointed out by the board at the oral proceedings.

Under Article 111(1), second sentence, EPC the board has discretion over whether to decide the case on its own or to remit it to the department whose decision has been appealed. Thus, a party has no absolute right to have an issue decided upon by two instances (see also Case Law of the Boards of Appeal of the European Patent Office, 8th edition 2016, IV.E.7.1 and 7.6.1).

In the present case, the unsuitability of the tests in documents (22) and (25) to show a stability or therapeutic improvement over the closest prior art was already discussed in the opposition proceedings (see appealed decision, page 17, lines 5-6 and last five lines) and was raised once more in the statement of grounds of appeal (see pages 14, 17 and 18). The board therefore came to the conclusion that remitting the case to the opposition division would be contrary to procedural economy and effectiveness and consequently exercised its discretion not to remit the case to the opposition division.

6. *Auxiliary request 1 - inventive step - Article 56 EPC*

Claim 1 of auxiliary request 1 specifies that the concentration of fluticasone ester is from 50 µg/ml to 5 mg/ml. This concentration range, calculated as percentage by weight, amounts to approximately 0.005 to 0.5 wt.%, a fact that was not contested by the respondent at the oral proceedings.

Knowing that the concentration of fluticasone propionate in commercial aqueous nasal sprays such as Flixonase® is of 0.05 wt.% (see document (3)), the limitation in auxiliary request 1 does not change the situation in terms of inventive step with regard to the main request. Hence, the formulation of claim 1 of auxiliary request 1 is likewise non-inventive.

7. *Auxiliary request 2 - inventive step - Article 56 EPC*

Claim 1 of auxiliary request 2 limits the fluticasone ester of the main request to fluticasone propionate.

The arguments against the inventive step of the main request were based on fluticasone propionate as the fluticasone ester. Therefore, the reasons why the formulation of claim 1 of the main request lacks inventive step apply *mutatis mutandis* to that of auxiliary request 2.

8. *Auxiliary request 3 - inventive step - Article 56 EPC*

Claim 1 of auxiliary request 3 results from the combination of the limitations of auxiliary requests 1 and 2. Thus, for the reasons set out for auxiliary requests 1 and 2, the formulation of claim 1 of auxiliary request 3 is also not inventive.

9. *Auxiliary request 4 - inventive step - Article 56 EPC*

Claim 1 of auxiliary request 4 differs from claim 1 of auxiliary request 3 in that azelastine is present in the form of azelastine hydrochloride. This limitation, however, does not represent any additional difference over the closest prior art because azelastine in example III of document (1) was also in the form of hydrochloride salt. Consequently, the formulation of claim 1 of auxiliary request 4 lacks inventive step too.

10. *Admission of auxiliary requests 5 and 6 - Article 13(1) RPBA*

Auxiliary requests 5 and 6 were filed towards the end of the oral proceedings before the board, allegedly in reaction to the board's view that the comparative examples in document (22) were not suitable to show a stability improvement for the claimed formulations. Among other amendments, claim 1 of both requests incorporated the thickener used in the formulation in column 1 of document (22), i.e. a combination of microcrystalline cellulose and carboxy methyl cellulose sodium. The basis for this amendment in the application as filed was, according to the respondent, the disclosure of the commercial products Avicel RC 591 and Avicel CL11 on page 4, paragraph 3 from the bottom, and examples 3 to 5, since Avicel products were well-known thickeners comprising a mixture of microcrystalline cellulose and carboxy methyl cellulose sodium.

The board noted that this amendment *prima facie* added subject-matter. The very fact that the application as filed did not contain any definition of the composition of Avicel products is problematic. But more importantly, even if the board accepted the

respondent's contention that Avicel products were generally known to contain a combination of microcrystalline cellulose and carboxy methyl cellulose sodium, the insertion of this generic definition into claim 1 clearly represents an unallowable generalisation of the specific components present in the products Avicel RC 591 and Avicel CL11. This is apparent from the fact that each Avicel product must contain a specific ratio of microcrystalline cellulose to carboxy methyl cellulose sodium and each of these two cellulose components must have specific properties in terms of e.g. chain length and derivatisation degree.

Consequently, in view of the formal issues raised *prima facie* by claim 1 of auxiliary requests 5 and 6 at such a late stage of the proceedings, the board decided not to admit them into the proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

M. Schalow L. Bühler

Decision electronically authenticated