Internal distribution code:

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

Datasheet for the decision of 13 April 2021

Case Number: T 1123/16 - 3.3.04

Application Number: 09725345.4

Publication Number: 2274009

IPC: A61K39/395, C07K16/24

Language of the proceedings: EN

Title of invention:
Methods of treatment

Patent Proprietor:
GlaxoSmithKline LLC

Opponents:
Urquhart-Dykes & Lord LLP
Cephalon, Inc.

Headword:
Eosinophilic bronchitis/GLAXO

Relevant legal provisions:
EPC Art. 56
RPBA Art. 12(4), 13

Keyword:
Inventive step - reasonable expectation of success (yes) - main request and auxiliary requests 1, 2 and 4
Late-filed auxiliary request 3 - admitted (no)

Decisions cited:
T 2506/12, T 0239/16, J 0004/03, J 0007/19

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

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

Case Number: T 1123/16 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 13 April 2021

Appellant: (Opponent 2)	Cephalon, Inc. 41 Moores Road Frazer, PA 19355 (US)
Representative:	D Young & Co LLP 120 Holborn London EC1N 2DY (GB)
Respondent: (Patent Proprietor)	GlaxoSmithKline LLC 251 Little Falls Drive Wilmington, DE 19808 (US)
Representative:	Goddard, Carolyn Janice GlaxoSmithKline Global Patents (CN925.1) 980 Great West Road Brentford, Middlesex TW8 9GS (GB)
Party as of right: (Opponent 1)	Urquhart-Dykes & Lord LLP The Podium 1 Eversholt Street London NW1 2DN (GB)
Representative:	Mitchell, Simon James Urquhart-Dykes & Lord LLP Euston House 24 Eversholt Street London NW1 1AD (GB)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 7 March 2016 rejecting the opposition filed against European patent No. 2274009 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chair B. Claes
Members: D. Luis Alves
R. Romandini

Summary of Facts and Submissions

I. Opponent 2 (appellant) filed an appeal against the opposition division's decision to reject the oppositions against European patent No. 2 274 009, entitled "*Methods of treatment*". The patent was granted on European patent application No. 09 725 345.4, which was filed as an international application published as WO 2009/120927.

II. Opponent 1 also filed an appeal against the decision of the opposition division. However, opponent 1 did not file any document which could qualify as a statement setting out the grounds of appeal. Consequently, this appeal has to be rejected as inadmissible (Article 108 EPC and Rule 101(1) EPC). Opponent 1 is therefore a party as of right to the appeal proceedings.

III. In the decision under appeal, the opposition division held that the patent as granted complied with the requirements of sufficiency of disclosure (Article 100(b) EPC) and that the claimed subject-matter did not extend beyond the content of the application as filed (Article 100(c) EPC), was entitled to the right of priority claimed, was novel and involved an inventive step (Article 100(a) EPC).

IV. With the statement setting out the grounds of appeal, the appellant contested the decision in relation to the findings on right to priority, novelty and inventive step and filed five documents. Further submissions were made with the letter dated 7 April 2017.

V. With the reply to the statement setting out the grounds of appeal, the patent proprietor (respondent) resubmitted the sets of claims of auxiliary requests 1 to 3 as filed on 25 March 2015 and filed one document.

VI. In response to the summons to oral proceedings, by letter dated 3 April 2020, the respondent submitted further arguments and filed one additional document and a set of claims as auxiliary request 3. Previous auxiliary request 3 was renumbered auxiliary request 4.

VII. The board issued two communications under Article 15(1) RPBA in preparation for the oral proceedings by which the parties were informed, *inter alia*, of the board's preliminary opinion that the subject-matter of claim 1 of each claim request did not involve an inventive step.

VIII. Both the appellant and the respondent made further submissions. The appellant submitted two documents.

IX. The oral proceedings took place by video conference. Opponent 1 was not represented, as announced beforehand.

At the end of the oral proceedings, the respondent withdrew auxiliary request 3. Subsequently, they requested that the board exercise its discretion to admit as an auxiliary request previous auxiliary request 3.

At the end of the oral proceedings, the Chair announced the board's decision.

X. Claim 1 of the patent as granted (**main request**) reads as follows:

"1. A composition comprising at least one neutralising humanised anti-human-IL-5 antibody for use in treating a human suffering from steroid-dependent eosinophilic bronchitis, characterised in that the steroid is prednisone and wherein the prednisone is reduced by at least about 90% in said human after treatment."

Claim 1 of **auxiliary request 1** (see section V.) contains the additional feature:

"and wherein the eosinophil level in said human is reduced to within normal limits after at least one dose of said composition, preferably wherein said eosinophil level remains within normal limits for at least 8 weeks after the last dose of said composition."

Claim 1 of **auxiliary request 2** (see section V.) reads as follows (difference from auxiliary request 1 emphasised by the board):

"1. A composition comprising at least one neutralising humanised anti-human-IL-5 antibody for use in treating a human suffering from steroid-dependent eosinophilic bronchitis, characterised in that the steroid is prednisone and wherein the prednisone is reduced by at least about 90% in said human after treatment and wherein the eosinophil level in said human sputum is reduced to within normal limits after at least one dose of said composition, preferably wherein said eosinophil level remains within normal limits for at least 8 weeks after the last dose of said composition."

Claim 1 of **auxiliary request 3** (see section VI.) reads as follows (difference from the main request emphasised by the board):

"1. A composition comprising at least one neutralising humanised anti-human-IL-5 antibody for use in treating a human suffering from steroid-dependent eosinophilic bronchitis and at least one additional disorder associated with excess eosinophil production, wherein the additional disorder is asthma, characterised in that the steroid is prednisone and wherein the prednisone is reduced by at least about 90% in said human after treatment."

Claim 1 of **auxiliary request 4** (see sections V. and VI.) differs from claim 1 of the main request in that it additionally comprises the feature:

"and wherein said at least one neutralising humanised anti-human-IL-5 antibody comprises a heavy chain comprising SEQ ID NO: 19 and a light chain comprising SEQ ID NO: 21."

XI. The following documents are referred to in this decision:

D1: "The Prednisone-Sparing Effect of Anti-IL-5 Antibody (SB-240563)" details of Clinical Trial NCT00292877

D2: Rothenberg *et al.*, NEJM, 358(12), 20 March 2008, 1215-1228

D5: Hargreave and Smith-Blackwell, Clin Exp Allergy, 34, 1806-1813, Abstracts British Society for Allergy and Clinical Immunology Annual Conference (12-14 July 2004): "Prednisone-sparing effect of anti-interleukin 5 in asthma" (page 1807 - abstract 4)

D6: Kips *et al.*, Am J Respir Crit Care Med, 167, 2003, 1655-1659

D7: Garrett *et al.*, J. Allergy Clin Immunol, 113(1), 2003, 115-119

D8: Adis R&D Profile, Drugs R D, 9 (2), 2008, 125-130

D9: "Phase III Study of Bosatria (mepolizumab) Showed Disease Control With Reduced Corticosteroid Use in Hypereosinophilic Syndrome" - Medical News Today (Press release of D8), 24 March 2008

D13: Flood-Page *et al.*, Am J Respir Crit Care Med, 176, 2007, 1062-1071

D15: Leckie *et al.*, Lancet, 356, 2000, 2144-2148

D16: Flood-Page *et al.*, Am J Respir Crit Care Med, 167, 2003, 199-204

D18: Korn *et al.* Am J Crit Care Med, 175, 2007, abstract A486

D21: Pizzichini *et al.*, Am J Respir Crit Care Med, 155, 1997, 1501-1508

D27: Paul O'Byrne, Am J Respir Crit Care Med, 176, 2007, 1059-1061

D39: Pizzichini *et al.*, Eur Respir J, 13, 1999, 15-21

D40: Lex *et al.*, Pedriatic Pulmonology, 42, 2007, 298-303

XII. The appellant's arguments relevant to the decision may be summarised as follows.

Main request - claim 1
Inventive step (Articles 56 and 100(a) EPC)

The objective technical problem, when considering the disclosure in document D1 as representing the closest prior art, was the provision of an effective treatment for eosinophilic bronchitis (EB) that avoided side effects of prednisone.

The disclosure in document D1 on its own already provided the skilled person with a reasonable expectation that the outcome measure of the clinical trial, i.e. the reduction in prednisone, would be achieved. Reference was made to the detailed definition in this document of the primary outcome, which required observing a prednisone-sparing effect in absence of exacerbations. A primary outcome was generally defined such that it corresponded to what was "reasonably expected to be achievable". This was a prerequisite for regulatory ethical approval of a clinical trial (see decisions T 2506/12 and T 1577/11).

The skilled person also had an expectation of success on the basis of other documents on file. Documents D21, D39 and D40 disclosed that prednisone achieved a reduction in sputum eosinophil levels. Documents D5, D6, D8, D13 and D15 disclosed that the same effect was achieved with an antibody to IL-5. The skilled person therefore expected that when treatment was based on an antibody to IL-5, less prednisone would be necessary to achieve a reduction in eosinophil levels. This was observed in hypereosinophilic syndrome (HES) patients, as disclosed in documents D2, D7 and D9.

None of the cited documents called into question the expectation of success that the skilled person derived from the disclosure in document D1.

Documents disclosing minimal or no effect on asthma symptoms upon treatment with an antibody to IL-5 did not contradict this expectation of success in treating patients as defined in the claim. Indeed, the ambitious objective of providing a treatment for asthma patients with an antibody to IL-5 did not succeed. Nevertheless, documents D13 and D27 foreshadowed the patient group suffering from asthma and EB as benefiting from the treatment. In spite of disclosing minimal effects of the anti-IL-5 therapy on lung function, document D13 also disclosed a reduction in exacerbations in patients with high sputum eosinophil levels (see pages 1066 and 1067 and page 1068, last paragraph). It was therefore reasonable to expect that treatment with an antibody to IL-5 would have an effect on exacerbations. Further studies were suggested to study the efficacy of the therapy in subgroups of patients with elevated eosinophil levels (see last paragraph). Document D27 likewise mentioned the patient subgroup with elevated eosinophils levels as patients who might benefit from the therapy (see last paragraph).

Therefore, the subject-matter of claim 1 was obvious to the skilled person in view of the disclosure in document D1.

Auxiliary requests 1, 2 and 4
Inventive step (Article 56 EPC) - claim 1

No arguments were submitted applying specifically to these requests.

Auxiliary request 3
Admittance into the appeal proceedings

This request was withdrawn at the oral proceedings and should not be admitted when re-submitted at a later point during the oral proceedings (see decision T 1790/06 and Case Law of the Boards of Appeal of the European Patent Office, 9th edition, page 1214).

The board's preliminary opinion had been negative, and therefore the board's decision on the main request was not a surprising development of events.

If the request were admitted, the reasons why it overcame the objections would be heard for the first time at the oral proceedings since no substantiation had been provided previously in the proceedings.

XIII. The respondent's arguments relevant to the decision may be summarised as follows.

Main request - claim 1
Inventive step (Articles 56 and 100(a) EPC)

The claimed subject-matter differed from the closest prior art represented by document D1 in that the prednisone dose could be reduced by 90% in patients after treatment. The technical effect associated with this distinguishing feature was a successful treatment with reduced side effects. The objective technical problem could thus be formulated as "the provision of a safer, more patient-compliant treatment for patients suffering from prednisone-dependent eosinophilic bronchitis".

The disclosure in document D1 alone did not lead the skilled person to expect that an antibody to IL-5 would be effective in reducing the prednisone dose in the treatment of patients with prednisone-dependent EB. The outcome of a clinical trial could not be predicted from the trial design.

Furthermore, the skilled person knew, from document D21 and document D40, that prednisone had an effect not only on eosinophil levels but also on asthma symptoms (see document D21, abstract, lines 12 and 13; document D40, page 300, right-hand column, first full paragraph). These two effects had to be regarded separately as was confirmed in document D21, disclosing that an effect on symptoms was observed before there was a decrease in sputum eosinophil levels. Thus, the decrease in sputum eosinophils was not responsible for the improvement in symptoms. From this, the skilled person would conclude that even if an antibody to IL-5 led to a decrease in sputum eosinophils, the patient would still require administration of prednisone to improve asthma symptoms. Therefore, when taking into account the state of the art, the skilled person would not have expected a reduction in prednisone.

Nor did the cited documents other than document D1 lead to an expectation of success. Documents D2 and D7 related to HES treatment and were therefore not relevant. An effect in this disorder could not be transferred to EB. The same applied to documents concerning asthma treatment. Furthermore, the latter disclosed no improvement in symptoms in spite of a decrease in eosinophil levels.

Documents D5 and D18 concerned single patients and therefore could not provide any incentive for the

skilled person. Furthermore, document D5 did not relate to patients as defined in the claim. It related to patients administered prednisone to control sputum eosinophilia whereas the patients as defined in the claim had sputum eosinophilia even under treatment with prednisone. Document D18 did not disclose any sputum eosinophils levels.

A prednisone-sparing effect in treatment of EB could moreover not be expected from documents disclosing a prednisone-sparing effect in treatment of asthma or HES with anti-IL-5 as the response to treatment and the eosinophils levels in sputum and blood were known not to correlate (see documents D2 and D6).

In decision T 239/16, the board held that the disclosure of the clinical trial provided the skilled person with an expectation of successful treatment "*unless he was dissuaded from this by the prior art*" (see Reasons 6.5, on page 31 of this decision) and concluded that the claimed treatment was obvious in view of this disclosure of the clinical trial because "*there is on the other hand no indication either that such treatment would fail*" (also in Reasons 6.5, on page 31).

In the current case, the skilled person knew that treatment with an antibody to IL-5 was not effective in asthma patients (see document D6, page 1658, first full paragraph; document D13, abstract and page 1067, sentence bridging the two columns; document D15, discussion, first paragraph, line 4; document D16, abstract, lines 16 to 18; and document D8 summarising the studies disclosed in documents D13, D15 and D16).

Even if at the time the clinical trial in document D1 had been approved, there would have been an expectation of successful treatment of the patients as defined in the claim that would not have been the case at the relevant date of the patent. Indeed, documents D13 and D27 removed any optimism that might still have existed. Document D13 reported on the results of a large scale study, contrary to the studies reported on in documents D6, D15 and D16, which were not powered to show clinical efficacy. It disclosed no effect on symptoms, despite the inclusion in the trial of patients with increased sputum eosinophil levels. Document D27 referred to prior studies which did not show efficacy of an antibody to IL-5 in the treatment of asthma as the "final nail in the coffin", clearly indicating that there was no expectation of success.

The clinical trial disclosed in document D1 was carried out in spite of a low expectation of success because of the need to reduce prednisone as acknowledged by the statement that "*At present there is no* [...] *drug which can have a prednisone-sparing effect*" (see document D1, page 2, "Detailed Description", first paragraph).

Moreover, unlike in the case underlying decision T 239/16, document D1 concerned a phase II clinical trial.

Therefore, the skilled person had no reasonable expectation of success. The subject-matter of claim 1 thus involved an inventive step.

Auxiliary requests 1, 2 and 4
Inventive step (Article 56 EPC) - claim 1

For each request, the "*additional feature yet further distinguished the claims*" from the cited documents. The arguments presented in relation to the main request applied equally to these requests.

Auxiliary request 3
Admittance into the appeal proceedings

The set of claims of this request could not be surprising to the appellant since the request had been filed earlier with the letter dated 3 April 2020.

Moreover, the feature added to claim 1 related to asthma patients, and precisely asthma treatment had also been the focus of the discussion at the oral proceedings.

The request overcame issues of inventive step since the claimed subject-matter defined a narrower patient group suffering from asthma in addition to EB.

XIV. The appellant requested that the decision under appeal be set aside and that the patent be revoked. Further they requested that auxiliary request 3 filed at the oral proceedings not be admitted into the proceedings.

The respondent requested that the appeal be dismissed or, alternatively, that the patent be maintained on the basis of auxiliary requests 1, 2 or 4 filed with the reply to the statement of grounds of appeal as auxiliary requests 1 to 3, respectively, or on the basis of auxiliary request 3 filed at the oral

proceedings before the board and identical to auxiliary request 3 filed with the letter of 3 April 2020.

Reasons for the Decision

1. The appeal complies with the requirements of Articles 106 to 108 and Rule 99 EPC and is admissible.

Absence of a party as of right at the oral proceedings

2. Opponent 1 was not represented at the oral proceedings, as announced beforehand. The board decided to continue the proceedings in absence of this duly summoned party (Rule 115(2) EPC and Article 15(3) RPBA).

Main request
Inventive step (Articles 56 and 100(a) EPC) - claim 1

Closest prior art

3. Claimed is a composition comprising a humanised antibody to human IL-5 for use in treating a human suffering from prednisone-dependent eosinophilic bronchitis (EB) (see section X.).

4. Document D1 describes a phase II clinical trial entitled "*The prednisone-sparing effect of anti-IL-5 antibody (SB-240563)*". The purpose of the clinical trial is "*to determine if the treatment with anti-IL-5 antibody has a prednisone-sparing effect in patients with symptomatic eosinophilic bronchitis (with or without asthma)*" (page 1, "Purpose"). The primary outcome measure is "*the prednisone sparing effect of SB-240563 versus placebo as indicated by the absolute*

and percentage dose reduction possible without a clinical exacerbation[...]" (page 2, first paragraph). Regarding the condition eosinophilic bronchitis (EB), this document states: "*Eosinophilic bronchitis, which is identified by quantitative sputum cell counts (eosinophils greater than 2%) is responsive to corticosteroid treatment. It occurs alone or in association with asthma or in some patients with chronic obstructive pulmonary disease (COPD)*".

5. Like the opposition division and the parties, the board considers the disclosure of this phase II clinical trial to constitute an appropriate starting point for assessing whether the claimed subject-matter involves an inventive step. Indeed, it concerns the treatment of patients with the same medical condition (i.e. steroid-dependent EB) using the same substance (i.e. a humanised antibody to IL-5) with the same objective (i.e. a reduction in prednisone administration).

Objective technical problem

6. The therapeutic application defined in the claim differs from the disclosure in document D1 in that (i) an effective treatment is not inferable from the document since it does not disclose any results of the clinical trial and (ii) whereas the claim specifies a minimum level of prednisone-sparing effect - 90% - none is specified in the document. This was not disputed by the parties.

7. It was undisputed that the patent discloses the results of the clinical trial as known from document D1, including a prednisone sparing effect as required by the claim. The technical effect of the above differences is that an effective treatment of

prednisone-dependent EB is provided allowing a 90% reduction of prednisone.

8. The objective technical problem may thus be formulated as the provision of an effective treatment of prednisone-dependent EB with reduced side effects.

Obviousness

9. The question of obviousness in the case at hand requires determining whether the state of the art provided the skilled person with a reasonable expectation that an anti-IL-5 antibody would be effective in the treatment of prednisone-dependent EB with less side effects.

10. The opposition division held that when starting from the disclosure in document D1, the skilled person had *no* reasonable expectation of solving the technical problem by providing a treatment with humanised antibody to IL-5. In their assessment of what the skilled person might have expected, the opposition division took into account documents other than document D1. However, the board holds that in this regard the disclosure in document D1 itself should also be considered.

11. In the board's view, the disclosure of a clinical trial with the same substance for the treatment of the same medical condition, and having the prednisone-sparing effect as the primary outcome measure of the clinical trial, there being no other distinguishing characteristics of the therapeutic application claimed than the efficacy, provides the skilled person with an expectation of success for the treatment (see also decision T 2506/12, Reasons 3.10 and decision T 239/16,

Reasons 6.5). It was therefore obvious for the skilled person to conduct the treatment in document D1 with a reasonable expectation of success, unless the state of the art provided the skilled person with reasons for not pursuing the solution envisaged in the clinical trial or, in other words, unless the state of the art provided the skilled person with an expectation of failure (see also decision T 2506/12, Reasons 3.11 and decision T 239/16, Reasons 6.5, second paragraph).

12. For the sake of completeness, the board notes that, contrary to the respondent's assertion, in decision T 239/16 the board in its reasoning did not give any relevance to the phase of the clinical trial. Instead the decision states: "*The board considers that the mere fact that an active agent selected from the group of bisphosphonates is being tested in a clinical study for the treatment of osteoporosis (as disclosed in document (55)) leads to an expectation of success, due to the fact that clinical studies are based on data obtained by pre-clinical testing both in vitro and in animals and require authority approval which takes ethical considerations into account.*" (see Reasons 6.5, second paragraph).

13. It therefore remains to be assessed whether the state of the art provided the skilled person with the expectation that the treatment would fail, as was argued by the respondent.

14. In a first line of argument, the respondent submitted that documents concerning hypereosinophilic syndrome (HES) or asthma treatment were not relevant to assess the skilled person's expectation of treating EB. The conclusions in these documents would not be applicable

to EB, being characterised by elevated eosinophil sputum levels.

15. In a second line of argument, the respondent submitted that documents concerning asthma treatment, such as documents D6, D8, D13, D15, D16 and D27, in fact showed that there was a negative expectation regarding a successful treatment based on an antibody to IL-5. The disclosure in documents D13 and D27 was considered particularly relevant in this regard.

16. This line of argument does not seem to be pertinent to the claim at hand because it does not require that the patients suffer from asthma. Effects observed in asthma patients are not necessarily indicative of any effect in EB patients since the role of eosinophils in asthma is not fully elucidated (see, for example, document D6, page 1568, left-hand column, first sentence of last paragraph and document D27, left-hand column, second paragraph, first sentence)). To the contrary, EB is characterised by a level of sputum eosinophils of at least 2% as well as its responsiveness to corticosteroids (see patent application on page 8, lines 14 to 17).

17. The above notwithstanding, an analysis of the cited documents also does not seem to support the respondent's argument.

18. D6 discloses a study aimed at evaluating the safety, biological activity and pharmacokinetics of an antibody to IL-5 in the treatment of patients with severe persistent asthma. As part of the assessment of biological activity, circulating and sputum eosinophils levels were determined (abstract). The effect of the treatment on sputum eosinophil levels was not

consistent. However, a decrease in sputum eosinophil levels was observed in three out of four patients with elevated sputum eosinophil levels (see page 1656, right-hand column, first full paragraph). The authors conclude that treatment with the antibody is safe. As concerns its therapeutic potential, they refer to the need for specifically designed efficacy trials (see abstract). As argued by the respondent, document D6 discloses that no improvement was observed in the treatment of severe asthma (see document D6, page 1658, first full paragraph). In this same paragraph, the authors indicate as possible reasons for this lack of efficacy that (i) the study was designed as a safety study and not powered to detect clinical efficacy and (ii) the dose and dosing frequency might have led to an insufficient reduction of eosinophils. Nevertheless, in this context they also state "[…] *the pathogenesis of severe persistent asthma shows considerable heterogeneity. It has been suggested that within the severe asthma phenotype, distinction can be made between an eosinophil-driven subgroup and a neutrophil-driven subgroup* […] *The patients included in this study were not selected for eosinophils in sputum or blood*". In conclusion, according to the authors of document D6, the absence of positive results on efficacy could be explained by factors other than the target of the therapy, i.e. IL-5. Moreover, the eosinophil level is also advanced as a characteristic possibly relevant to the efficacy. The board can thus not derive from the disclosure in document D6 that an antibody to IL-5 would not be suitable for the treatment of EB.

19. Document D15 is concerned with allergic asthma. Treatment with an antibody to IL-5 resulted in a decrease in blood and sputum eosinophils. The role of eosinophils in the late asthmatic response is

questioned because the treatment did not provide medical benefit upon allergen challenge (abstract and discussion, first full paragraph, line 4). Document D16 elaborates on the study reported in document D15. It concludes that there were "*no significant changes in clinical measures of asthma*" (see abstract, lines 16 to 28). This result is attributed to less of a reduction in airway eosinophil level than achieved with oral corticosteroids. The authors suggest larger studies to assess the efficacy at the level of patient subgroups differing in the level of airway obstruction or tissue eosinophilia (see page 201, left-hand column, third paragraph and paragraph bridging pages 201 and 202). From this disclosure, the board cannot derive an expectation that a treatment of EB, which is characterised by elevated eosinophil sputum levels, would not be successful.

20. Document D8 merely reviews studies such as those disclosed in documents D15 and D13 so that it does not add to the above conclusions on the assessment of the skilled person's expectation of success.

21. Document D13 concerns the treatment of asthma patients with persistent symptoms despite inhaled corticosteroid therapy. According to the authors of this article, no clinical benefit was demonstrated with treatment with an antibody to IL-5 despite significant reductions in blood and sputum levels (see abstract and page 1067, paragraph bridging the two columns). The authors note that the reason for different responses in tissue eosinophils with different diseases is not known, and they suggest further studies to determine whether the therapy would be useful in patient subgroups, namely those with persistent airway eosinophilia: "*this study does not exclude that specific targeting of those with*

persistent eosinophilic disease might identify those likely to respond to anti-IL-5, although further studies would be required to clarify this point" (see page 1068, last paragraph and page 1069, last paragraph). Document D27 summarises studies on asthma Il-5 antibody therapies, including a review of the disclosure in document D13. It notes the results as discussed above but nevertheless concludes with the following outlook: "*Anti-IL-5 has proven to be useful in managing hypereosinophilic syndrome (12, 13) and may also be shown to be beneficial in clinical trials in patients with asthma with airway eosinophilia associated with poor control, when corticosteroids are reduced. The results of these trials, which are underway, are eagerly awaited, because they have implications not only for the possible role of anti-IL-5 as a therapy for asthma but also in clarifying the role of airway eosinophils in its pathobiology*." (see last paragraph).

22. Thus, documents D13 and D27 do not address the treatment of EB. Furthermore, concerning the treatment of asthma, they emphasise that the subgroup of patients with elevated levels of eosinophils may benefit from treatment.

23. In view of the above considerations, the skilled person had no reason to expect that the treatment described in document D1 would not succeed. The solution provided in the claim, specifying the level of reduction in prednisone to be 90%, is a consequence of pursuing the treatment described in document D1, for which the skilled person had a reasonable expectation that a prednisone reduction would be achieved without exacerbations. Therefore, the specific level of reduction of 90% recited in the claim does not play a

role in the assessment of what the skilled person would do when faced with the problem formulated above, i.e. the provision of an effective treatment for prednisone-dependent EB with less side effects.

24. In view of the above considerations, the subject-matter of claim 1 is obvious to the skilled person and thus lacks an inventive step.

Auxiliary requests 1 and 2
Inventive step (Article 56 EPC) - claim 1

25. Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that it specifies additionally that the eosinophil level in the patient is reduced to normal levels after administration of one or more doses of the composition (see section X.). Claim 1 of auxiliary request 2 further specifies that the eosinophil level refers to sputum eosinophils.

26. As stated for claim 1 of the main request in respect of the specific level of prednisone reduction recited in the claim, the level of reduction in eosinophil levels in the current claim results from pursuing the treatment described in document D1, for which the skilled person had a reasonable expectation that a prednisone reduction would be achieved without exacerbations (see points 4. and 11.). Based on this document, the skilled person likewise had a reasonable expectation that the treatment would result in a reduction in eosinophil levels since one of the secondary measurement outcomes of the clinical trial disclosed in document D1 is precisely the level of sputum eosinophils (see page 2).

27. The respondent has not provided arguments for this feature, merely submitting that it further distinguished the claimed subject-matter from the cited art.

28. Therefore, the above conclusion with regard to inventive step applies equally, and the subject-matter of claim 1 of auxiliary requests 1 and 2 does not meet the requirements of Article 56 EPC.

Auxiliary request 4
Inventive step (Article 56 EPC) - claim 1

29. Claim 1 of this request differs from claim 1 of the main request in that it specifies the amino acid sequence of the heavy and light chains of the anti-IL-5 antibody (see section X.).

30. The respondent did not present arguments why this specific antibody for the treatment as defined in the claim involved an inventive step.

31. Therefore, the board's reasoning with respect to the main request, which is not restricted to a particular anti-IL-5 antibody, is applicable.

32. In conclusion, the subject-matter of claim 1 of auxiliary request 4 does not comply with the requirements of Article 56 EPC.

Auxiliary request 3
Admittance into the appeal proceedings

33. The appellant withdrew auxiliary request 3 at the oral proceedings. The intention to withdraw the request was not only stated but also confirmed when the appellant

was asked about it by the Chair. The withdrawal was therefore unequivocal.

34. Subsequently, when the Chair was about to ask the parties to state their final requests, the appellant informed the board that they intended to resubmit auxiliary request 3. Asked again by the board about the meaning of this statement, the appellant clarified that they were not arguing that the withdrawal was made by mistake and did not reflect their true intention. Instead, they had changed their mind, and for this reason they wanted to resubmit the withdrawn request.

35. The EPO must be able to rely on procedural statements of the parties made in the course of a proceedings (see decisions J 4/03, Reasons 12; J 7/19, Reasons 7). Statements made at the oral proceedings are not excepted from this principle. Therefore, the board had to consider the auxiliary request concerned as if it were filed for the first time during the oral proceedings and at a very late stage. Given this, the board could not consider the requests for two reasons.

35.1 First, the request could have been filed earlier. The evidence for this is that it was indeed filed but withdrawn during the appeal proceedings. The criteria governing the admittance of a new request filed with the statement of grounds in accordance with the case law concerning Rule 12(4) RPBA 2007 shall apply *a fortiori* to the admittance of new requests filed later on in the proceedings, the board having discretion to consider or not the new request.

35.2 Second, nothing happened during the oral proceedings and in particular after the third auxiliary request was withdrawn which could have justified the filing of a

new request. The filing of the auxiliary request was not a reaction to any new objection of the board or new attack of the opponent which the board considered or anything else which happened in the proceedings after the request was withdrawn. It was simply the result of a change of mind of the appellant.

36. In cases where an applicant or appellant makes a decision and takes a procedural step without considering all the relevant circumstances, this party must bear the consequences of its decision (see also decision J 7/19, Reasons 7), even if it realises *ex post* that another choice would have better suited its interests. Beyond the exceptional case of a mistake eligible for correction under Rule 139 EPC, all parties to proceedings before the EPO are bound by their statements.

37. In view of the above considerations, the board decided not to admit the auxiliary request 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 Chair:

I. Aperribay B. Claes

Decision electronically authenticated