Internal distribution code:

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

Datasheet for the decision of 8 December 2020

Case Number: T 2674/17 - 3.3.04

Application Number: 10153282.8

Publication Number: 2253644

IPC: A61K38/17, C07K14/705, C07K16/28

Language of the proceedings: EN

Title of invention:
Compositions and methods for producing a composition

Patent Proprietor:
Bristol-Myers Squibb Company

Opponents:
df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte ParG mbB
Potter Clarkson LLP

Headword:
Method for obtaining a composition comprising CTLA4-Ig molecules/BRISTOL-MYERS SQUIBB

Relevant legal provisions:
EPC Art. 113(2)
RPBA Art. 13

Keyword:
New main request - admitted (no);
Basis of decision - text submitted or agreed by the patent proprietor (no)

Decisions cited:

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 2674/17 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 8 December 2020

Appellant: (Patent Proprietor)	Bristol-Myers Squibb Company Route 206 and Province Line Road Princeton, NJ 08543 (US)
Representative:	Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
Respondent I: (Opponent 1)	df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte ParG mbB Fünf Höfe Theatinerstrasse 16 80333 München (DE)
Representative:	Dörries, Hans Ulrich df-mp Fünf Höfe Theatinerstrasse 16 80333 München (DE)
Respondent II: (Opponent 2)	Potter Clarkson LLP The Belgrave Centre Talbot Street Nottingham NG1 5GG (GB)
Representative:	Potter Clarkson The Belgrave Centre Talbot Street Nottingham NG1 5GG (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 29 September 2017 revoking European patent No. 2253644 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chair	G. Alt
Members:	R. Morawetz
	R. Romandini

Summary of Facts and Submissions

I. The appeal of the patent proprietor (appellant) lies from the opposition division's decision revoking European patent No. 2 253 644 ("the patent"). The patent, entitled "*Compositions and methods for producing a composition*", is derived from European patent application No. 10 153 282.8 ("the application as filed" or "the application"), which was filed as a divisional application of European patent application No. 06 848 052.4 ("the earlier application").

II. Two oppositions were filed. The patent was opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), and under Article 100(b) and Article 100(c) EPC.

III. In reply to the notices of opposition, the appellant maintained the claims as granted as their main request and filed sets of claims of auxiliary requests 1 to 5. The opposition division arranged oral proceedings and issued a communication setting out its preliminary opinion. In response, the appellant by letter of 27 June 2017 filed an amended main request (consisting of claim 1 as granted) and auxiliary requests 1 to 3. These requests replaced all the pending requests. At the beginning of the oral proceedings, the appellant withdrew auxiliary requests 2 and 3 (see minutes drawn up by the opposition division, page 2, first paragraph). After the opposition division announced that the subject-matter of claim 1 of the main request lacked inventive step, the appellant withdrew auxiliary request 1. Furthermore, the appellant stated that they

had no further requests (*ibid.*, page 3, second to fourth paragraphs).

IV. The opposition division held that the subject-matter of the sole claim of the main request filed with the letter of 27 June 2017 met the requirements of Articles 123(2), 76(1) and 54(2) EPC but lacked inventive step (Article 56 EPC), and revoked the patent.

V. With their statement of grounds of appeal, the appellant maintained the main request underlying the decision under appeal and filed auxiliary requests 1 to 9, each consisting of a single claim. The appellant provided arguments to the effect that the subject-matter of claim 1 of the main request and of auxiliary requests 1 to 9 involved an inventive step. They argued that the patent taught a method for purifying CTLA4-Ig molecules from a liquid cell culture so that the purified CTLA4-Ig was substantially free of MCP-1. The problem to be solved was defined as the provision of a method for obtaining a purified high quality CTLA4-Ig composition that was pharmaceutically acceptable. The appellant submitted that placing the steps of the method in the right order while selecting particular types of columns was key to controlling both product quality and process yield.

Claim 1 of the main request read as follows:

"1. Method for obtaining a composition comprising an isolated population of CTLA4-Ig molecules from a liquid culture medium, the medium comprising an initial population of CTLA4-Ig molecules, wherein (1) CTLA4-Ig molecules of the initial population have one or more sialic acid residues, (2) the number of sialic acid

residues per CTLA4-Ig molecule varies within the initial population, (3) the initial population comprises CTLA4-Ig dimer and high molecular weight aggregate, and (4) the liquid culture medium contains MCP-1, the method comprising:

(i) harvesting the liquid culture medium from a culture of mammalian cells expressing CTLA4-Ig molecules;
(ii) separating the CTLA4-Ig molecules from cellular components;
(iii) using column chromatography to reduce MCP-1 content in the composition;
(iv) using column chromatography to separate CTLA4-Ig dimers from CTLA4-Ig high molecular weight aggregates; and
(v) using column chromatography to separate the CTLA4-Ig molecules into two or more fractions, wherein at least one fraction has a greater molar ratio of sialic acid to CTLA4-Ig molecules compared to at least one other fraction,
(vi) wherein steps (ii), (iii), (iv) and (v) are carried out simultaneously or in any order, so as to obtain said composition."

VI. Opponent 1 and opponent 2 are respondent I and respondent II respectively (or "respondents") in these appeal proceedings. In their replies to the appellant's statement of grounds of appeal, they maintained an objection under Article 123(2) EPC against the subject-matter of claim 1 of the main request regarding, *inter alia*, the absence from step (iv) of a limitation disclosed in paragraph [0203] of the application as filed. They further submitted that the opposition division's decision was correct with respect to lack of inventive step of claim 1 of the main request. With respect to auxiliary requests 1 to 9, the respondents

submitted, *inter alia*, that the appellant's defence strategy had changed considerably with respect to the first-instance proceedings. Any claim amendment that was associated with the newly-presented argument that the composition must be substantially free of MCP-1 should not be admitted into the proceedings because it could have been presented earlier.

VII. The board arranged oral proceedings as requested by the parties.

VIII. In response, both respondents indicated that they would not attend.

IX. In July 2020, the board issued a communication pursuant to Article 15(1) RPBA setting out its preliminary assessment of substantive and legal matters concerning the appeal. In this communication, the parties were informed, *inter alia*, with respect to the requirements of Article 123(2) EPC of claim 1 of the main request that "*the board is inclined to agree with the respondents that a limitation disclosed in paragraph [00203] is missing from step (iv) of claim 1*". The board further noted that the appellant had "*made no submissions on this point*" in the appeal proceedings. With respect to inventive step of claim 1 of the main request, the board noted that in its opinion "*the problem formulated by the appellant - the provision of a method for obtaining a purified high quality CTLA4-Ig composition that is pharmaceutically acceptable - is not solved by the claimed subject-matter because, as also submitted by the appellant, that would require placing the steps of the method in the right order and selecting particular types of columns*" and that "*the appellant's arguments in support of non-obviousness do not apply to claim 1 given that*

neither the steps nor the particular types of columns are indicated in claim 1."

X. In response, by letter dated 20 November 2020, the appellant filed a new main request consisting of a sole claim which replaced all the claim requests on file. They submitted that the objective technical problem of "providing a method for obtaining a purified high quality CTLA4-Ig composition that is pharmaceutically acceptable" was solved by the amended claim because it required the method to be carried out so as to obtain a composition that was indisputably a "purified high quality CTLA4-Ig composition that is pharmaceutically acceptable" (emphasis in the original).

Claim 1 reads as follows (amendments with respect to claim 1 of the previous main request are indicated):

"1. Method for obtaining a composition comprising an isolated population of CTLA4-Ig molecules from a liquid culture medium, the medium comprising an initial population of CTLA4-Ig molecules, wherein (1) CTLA4-Ig molecules of the initial population have one or more sialic acid residues, (2) the number of sialic acid residues per CTLA4-Ig molecule varies within the initial population, (3) the initial population comprises CTLA4-Ig dimer and high molecular weight aggregate, and (4) the liquid culture medium contains MCP-1, the method comprising:

(i) harvesting the liquid culture medium from a culture of mammalian cells expressing CTLA4-Ig molecules;
(ii) separating the CTLA4-Ig molecules from cellular components;
(iii) using column chromatography to reduce MCP-1 content in the composition;

(iv) using column chromatography to separate CTLA4-Ig dimers from CTLA4-Ig high molecular weight aggregates so as to obtain fractions of CTLA4-Ig molecules having different sialic acids contents; and
(v) using column chromatography to separate the CTLA4-Ig molecules into two or more fractions, wherein at least one fraction has a greater molar ratio of sialic acid to CTLA4-Ig molecules compared to at least one other fraction, wherein steps (ii), (iii), (iv) and (v) are carried out simultaneously or in any order, so as to obtain said composition wherein:

the CTLA4-Ig molecules comprise one or more polypeptides having SEQ ID NO: 2, 5, 6, 7, 8, 9, or 10;
the bioburden is less than 100 cfu/mL;
the amount of residual recombinant protein A is less than or equal to 9.5 ng/mL;
the amount of DNA is less than or equal to 20 pg/mL;
the amount of Triton X-100 is less than or equal to 4 µg/mL;
the molar ratio of N-acetyl neuraminic acid (NANA) to CTLA4-Ig molecules is from 8.0 to 11.9;
the amount of CTLA4-Ig high molecular weight species is less than or equal to 2.0 area percent;
the amount of Chinese hamster ovary host cell proteins (CHOP) is less than or equal to 95 ng/mL; and
the amount of monocyte chemotactic protein 1 (MCP-1) is less than or equal to 9.5 ng/mL."

XI. In a further communication pursuant to Article 15(1) RPBA, the board informed the parties that it was inclined not to admit the new main request into the appeal proceedings.

XII. The oral proceedings before the board took place as scheduled in the absence of the duly-summoned

respondents I and II pursuant to Rule 115(2) EPC and Article 15(3) RPBA. At the end, the Chair announced the board's decision.

XIII. The appellant's arguments, submitted in writing and during the oral proceedings and as far as relevant to the present decision, are summarised as follows:

New main request

Admittance into the appeal proceedings (Article 13 RPBA 2007)

The claim was amended in two respects. The first amendment, to step (iv) of claim 1, was made so as to match the wording of paragraph [00203] of the application, and the second so as to characterise the final composition in greater detail by reciting the parameters given in Table 15 of Example 29 on page 398 of the application.

These amendments *prima facie* overcame the objections raised in the board's communication and did not give rise to new objections.

Table 15 of the application disclosed the product as such and the combination of this disclosure with the method of claim 1 met the requirements of Article 123(2) EPC.

The claimed subject-matter now solved the objective technical problem of providing a purified high-quality CTLA4-Ig composition that was pharmaceutically acceptable.

The filing of the new request was triggered by recent developments in the appeal case relating to the earlier application. Procedural economy was served by replacing all the claim requests on file by one claim request.

The respondents had not raised any objection to the admittance of this request into the appeal proceedings.

XIV. The appellant requested that the main request filed by letter of 20 November 2020 be admitted into the appeal proceedings and that the decision under appeal be set aside and the patent be maintained on the basis of claim 1, the sole claim, of the new main request.

XV. The respondents requested in writing that the appeal be dismissed.

Reasons for the Decision

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

2. An amended version of the Rules of Procedure of the Boards of Appeal (RPBA 2020) entered into force on 1 January 2020. The transitional provisions are set out in Article 25 RPBA 2020. In the case at hand, the parties were notified of the summons to oral proceedings before 1 January 2020. Therefore Article 13(2) RPBA 2020 does not apply. Instead, Article 13 RPBA 2007 continues to apply.

New main request

Admittance into the appeal proceedings (Article 13 RPBA 2007)

3. This request was filed two weeks before the oral proceedings, and almost four months after the board had expressed its preliminary opinion with respect to the claim requests submitted with the appellant's statement of grounds of appeal, see sections IX. and X. above.

4. Claim 1 of the new main request was amended vis-à-vis claim 1 of the previous main request in two respects, see section X. above. First, step (iv) of the method was amended so as to match the wording of paragraph [00203] of the application by including a reference to obtaining fractions of CTLA4-Ig molecules having different sialic acid contents (first amendment). Second, based on Table 15 of Example 29 of the application, the parameters characterising the final composition were defined in greater detail (second amendment).

5. The combination of features claimed had not been claimed before, and thus represented an amendment to the appellant's case. Admittance of the new main request was thus governed by the provisions of Article 13 RPBA 2007.

6. Pursuant to Article 13(1) RPBA 2007, an amendment to a party's case after it has filed its grounds of appeal or reply may be admitted and considered at the board's discretion. The board, when exercising its discretion, must consider, *inter alia*, the need for procedural economy.

7. Additional criteria are used by the boards of appeal when considering the admittance of new requests filed after the oral proceedings have been arranged, as in the present case. These are (i) if sound reasons exist for filing the request so far into the proceedings, (ii) if the request does not extend the scope of discussion as determined by the grounds of appeal and the respondents' replies, and (iii) if the request is clearly and obviously allowable in the sense that it is immediately apparent to the board, with little investigative effort on its part, that the amendments made successfully address the issue raised without giving rise to new ones (see Case Law of the Boards of Appeal, 9th edition 2019, V.A.4.5.1 a)).

8. With respect to criterion (i) above - whether or not sound reasons existed for filing a request so far into the proceedings - the board noted as regards the first amendment that it addressed an objection under Article 123(2) EPC that corresponded to an objection made during the opposition proceedings and that was maintained by the respondents in their replies to the statement of grounds of appeal, see section VI. above, and that was remarked upon in the board's preliminary opinion, see section IX. above, but that had not been addressed by the appellant before, see section IX. above. Considering these circumstances, there was no sound reason apparent why a reaction to this objection had not been filed earlier in the appeal proceedings.

9. This was also true with respect to the second amendment. Indeed, it aimed at addressing the objection of lack of inventive step, and thus an issue which had

already been in the proceedings before the opposition division. Inventive step had also been one of the reasons that had led to the present patent being revoked.

10. As to criterion (ii) above - whether or not the request extended the scope of discussion as determined by the grounds of appeal and the respondents' replies - the board noted that the definition of the composition newly introduced into claim 1 by the second amendment, see point 4. above, extended the scope of discussion as determined by the grounds of appeal and the respondents' replies for the following reasons.

11. While the claim requests submitted with the statement of grounds of appeal defined the steps of the method of claim 1 in detail, the composition comprising an isolated population of CTLA4-Ig molecules obtained as a result of the method was at most defined as being "*substantially free of MCP-1*". As a consequence of the second amendment, the board in these appeal proceedings was confronted for the first time with a claim which characterised the composition in great detail, see section X. above. This change in the claimed subject-matter necessarily extended the scope and framework of the discussion with regard to at least Article 123(2) EPC vis-à-vis that determined by the statement of grounds of appeal and the replies, see also points 14. and 15. below.

12. That the board had considered the appellant's arguments with respect to inventive step submitted in their statement of grounds of appeal not persuasive, see section IX. above, did not justify the filing of a request which required consideration of completely

different subject-matter and a considerably different line of argument, see section X. above, either.

13. Regarding criterion (iii) above - whether or not the request was clearly and obviously allowable in the sense that it was immediately apparent to the board, with little investigative effort on its part, that the amendments made successfully addressed the issue raised without giving rise to new ones - the board considered that this was not so, at least as far as the requirements of Article 123(2) EPC were concerned, for the following reasons.

14. Table 15 of the application disclosed the characteristics of a product obtained using specific cells (CHO cells) and specific chromatography steps in a particular order (see Examples 28 and 29), whereas claim 1 disclosed that the same product could also be obtained by the general method recited in that claim.

15. Since it was not directly and unambiguously derivable from the application as filed as a whole that a composition as characterised in claim 1 was obtainable by any other method than that disclosed in Examples 28 and 29, and in particular not by carrying out a method comprising steps (ii), (iii), (iv) and (v) as defined in claim 1 simultaneously or in any order "*so as to obtain*" this composition, combining the product characteristics according to Table 15 of the application with the general method steps of claim 1 was likely to result in new technical information.

16. Taken together, the board concluded that the new main request was filed late in the appeal proceedings without sound reasons. Further, it changed the appellant's case so that it was likely to extend the

scope of discussion as determined by the grounds of appeal and the respondents' replies. Finally, it was not immediately apparent to the board that the amendments made successfully addressed the issues raised without giving rise to new ones.

17. The appellant's argument that the admittance of the late-filed new main request served procedural economy because it replaced all the other requests on file was not persuasive in the present circumstances since the request as such, were it to be admitted, raised new issues, see previous points, which, if they had to be dealt with, would jeopardise procedural economy.

18. Against this background, the further two aspects referred to by the appellant, i.e. the absence of an objection to admittance by the respondents and that filing the request at this particular point in time had been triggered by the board's decision on clarity in the appeal case relating to the earlier application, decision T 2268/17 of 20 October 2020, could not persuade the board to exercise its discretion in favour of admitting the request. As to the first aspect, the board considered that the provisions and procedural principles mentioned (see points 6. and 7. above) also applied in the absence of an objection to admittance by another party, e.g. in *ex parte* proceedings. As to the second aspect, the board considered that the two proceedings - the one concerning the earlier application, and the one concerning the patent in suit - were independent of each other.

19. In view of all the above considerations, the board, exercising its discretion pursuant to Article 13 RPBA 2007, decided not to admit the new main request into the appeal proceedings.

Conclusion

20. As the appellant had replaced all the previous claim requests with the new main request, in view of the non-admittance of this request by the board there is no further text approved by the appellant within the meaning of Article 113(2) EPC in the appeal proceedings on the basis of which a patent might be granted. Accordingly, the decision under appeal revoking the patent cannot be set aside and the appeal must be dismissed.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

B. ter Heijden G. Alt

Decision electronically authenticated