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Datasheet for the decision of 8 June 2022

Case Number: T 1771/19 - 3.3.04

Application Number: 08792022.9

Publication Number: 2174667

IPC: A61K39/00, A61K31/00, C07K16/28

Language of the proceedings: EN

Title of invention:
Agent for treatment of ophthalmia containing interleukin-6 receptor inhibitor as active ingredient

Patent Proprietors:
Osaka University
Kyushu University, National University Corporation
Chugai Seiyaku Kabushiki Kaisha

Opponent:
Regeneron Pharmaceuticals, Inc.

Headword:
Ocular inflammatory diseases/OSAKA UNIVERSITY

Relevant legal provisions:
EPC Art. 123(2)

This datasheet is not part of the Decision
It can be changed at any time and without notice

Keyword:
Main request and auxiliary requests 1 to 5 - Amendments - allowable (no)

Decisions cited:
G 0002/10

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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 1771/19 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 8 June 2022

Appellant: (Opponent)	Regeneron Pharmaceuticals, Inc. 777 Old Saw Mill River Road Tarrytown NY 10591 (US)
Representative:	J A Kemp LLP 80 Turnmill Street London EC1M 5QU (GB)
Respondent: (Patent Proprietor 1)	Osaka University 1-1, Yamadaoka Suita-shi Osaka 565-0871 (JP)
Respondent: (Patent Proprietor 2)	Kyushu University, National University Corporation 10-1, Hakozaki 6-chome Higashi-ku Fukuoka-shi, Fukuoka 812-8581 (JP)
Respondent: (Patent Proprietor 3)	Chugai Seiyaku Kabushiki Kaisha 5-1 Ukima 5-chome Kita-ku Tokyo 115-8543 (JP)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB Siebertstrasse 3 81675 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 24 April 2019 concerning maintenance of the European Patent No. 2174667 in amended form.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	D. Luis Alves
	L. Bühler

Summary of Facts and Submissions

I. European patent EP 2 174 667, entitled "*Agent for treatment of ophthalmia containing interleukin-6 receptor inhibitor as active ingredient*", was granted on European patent application No. 08 792 022.9, filed as an international application published as WO 2009/014263. In the following, "the application as filed" refers to the English translation of the international application as filed upon entry into the regional phase before the EPO.

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

III. The opposition division decided that, account being taken of the amendments in the form of the main request, the patent and the invention to which it related met the requirements of the EPC.

IV. The opponent (appellant) filed an appeal against this decision.

V. With the statement setting out the grounds of appeal, the appellant submitted documents D28 to D30. Further, the appellant submitted arguments to the effect that the claims were not clear (Article 84 EPC) and that their subject-matter extended beyond the content of the application as filed (Article 123(2) EPC), was not sufficiently disclosed (Article 83 EPC), lacked novelty (Article 54 EPC) and did not involve an inventive step (Article 56 EPC).

VI. With the reply to the statement setting out the grounds of appeal, the patent proprietors (respondents) filed sets of claims of a main request and of auxiliary requests 1 to 5, all identical to the claim requests filed in opposition proceedings. They additionally submitted documents D31 and D31a, as well as arguments addressing each of the issues contested by the appellant.

VII. The board appointed oral proceedings and, in a communication pursuant to Article 15(1) RPBA, informed the parties of its preliminary opinion that, *inter alia*, the subject-matter of claim 1 of each request extended beyond the content of the application as filed (Article 123(2) EPC).

VIII. In reply the respondents submitted further arguments.

IX. By letter dated 3 May 2022, the appellant informed the board that it would not attend the oral proceedings.

X. The oral proceedings took place in the absence of the appellant.

At the oral proceedings, the respondents renumbered the auxiliary requests such that auxiliary request 1 corresponds to auxiliary request 5 as filed with the reply to the statement of grounds of appeal, and auxiliary requests 2 to 5 correspond to auxiliary requests 1 to 4, respectively, as filed with the reply to the statement of grounds of appeal.

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

XI. Claim 1 of the **main request** reads as follows:

"1. A therapeutic and/or prophylactic agent which comprises an anti-IL-6 receptor antibody as an active ingredient for use in treating and/or preventing autoimmune uveitis."

Claim 1 of **auxiliary request 1** reads as follows (emphasis by the board):

"1. A therapeutic agent which comprises an IL-6 receptor inhibitor as an active ingredient for use in treating autoimmune uveitis, wherein the IL-6 receptor inhibitor is an anti-IL-6 receptor antibody, **wherein said anti-IL-6 receptor antibody suppresses differentiation of CD4-positive T cells into TH17 cells**."

Claim 1 of **auxiliary request 2** is identical to claim 1 of the main request except for the insertion of the following feature at the end of the claim:

"wherein said anti-IL-6 receptor antibody suppresses differentiation of CD4-positive T cells into TH17 cells."

Claim 1 of **auxiliary request 3** is identical to claim 1 of the main request except that "and/or prophylactic agent" and "and/or preventing" have been deleted.

Claim 1 of **auxiliary request 4** is identical to claim 1 of auxiliary request 2 except that "and/or prophylactic agent" and "and/or preventing" have been deleted.

Claim 1 of **auxiliary request 5** reads as follows:

"1. A therapeutic agent which comprises an IL-6 receptor inhibitor as an active ingredient for use in treating autoimmune uveitis, wherein the IL-6 receptor inhibitor is an anti-IL-6 receptor antibody."

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

D23: Chi *et al.*, J Allergy Clin Immunol 119(5), 2007, pages 1218-1224.

D26: Gery *et al.*, "The Molecular Pathology of Autoimmune Diseases", 2nd edn., Chapter 57, pages 978-998.

D27: Caspi *et al.*, J Immunol 140(5), 1988, pages 1490-1495.

D28: NHS "Overview Behçet's disease", NHS, https://www.nhs.uk/conditions/behcets-disease/, 5 pages.

D29: Norose *et al.*, Invest Ophthalmol Vis Sci 35(1), 1994, pages 33-39.

D30: Hohki *et al.*, Exp Eye Res 91, 2010, pages 162-170.

D31a: English translation of S. Kotake, Jpn J Clin Immun 17(6), 1994, pages 847-849.

XIII. The appellant's arguments, where relevant to this decision, may be summarised as follows:

Main request - claim 1
Amendments - Article 123(2) EPC

The feature "autoimmune uveitis" had no basis in the application as filed.

The claims encompassed human treatment, but the examples and paragraph [0011] of the application as filed referred to an animal model and thus did not disclose treatment in humans.

The only mention of "autoimmune" in the application as filed was in the context of the experimental autoimmune uveitis (EAU)-induced mouse model (paragraphs [0011] and [0087]). As acknowledged by the opposition division and the respondents during the opposition proceedings, the EAU model was used to model autoimmune uveitis as well as other autoimmune diseases and ocular inflammatory diseases. Therefore, "autoimmune uveitis" could not be a direct and unambiguous implication of the disclosure of the animal model.

Such an interpretation would have been inconsistent with the disclosure in the application as a whole, which presented the EAU model as a model for all types of ocular inflammatory diseases (paragraph [0012]). When the application mentioned specific ocular inflammatory diseases, no reference was made to "autoimmune" or to "autoimmune uveitis". The only mention of specific types of uveitis was based on their locations (paragraphs [0012] and [0085] and claim 5).

The common general knowledge of the skilled person could be used only to interpret the disclosure in the application as filed. It should not be used to supplement or change it.

Auxiliary requests 2 to 5 - claim 1
Amendments - Article 123(2) EPC

The arguments submitted in the context of the main request applied equally to the auxiliary requests.

XIV. The respondents' arguments, where relevant to this decision, may be summarised as follows:

Main request - claim 1
Amendments - Article 123(2) EPC

The application as filed focused on autoimmune uveitis (paragraphs [0010] to [0012], [0085] and [0087], and example 1). Moreover, a therapeutic effect, as mentioned in paragraph [0011], was to be understood as referring to humans.

The terms "panuveitis", "intermediate" and "anterior uveitis" in item [5] of paragraph [0012] referred to the location of the inflammation but did not imply that these did not refer to autoimmune uveitis.

The application as filed was to be read with the common general knowledge of the skilled person. Experimental autoimmune uveitis in mice was an established animal model for autoimmune uveitis.

An example of autoimmune uveitis disease was Vogt-Koyanagi-Harada (VKH) disease (see document D26, section 8.4 and document D23, page 1218, left-hand column, "Background" and right-hand column, second paragraph). Document D27 disclosed EAU as a model for autoimmune diseases of the eye and in particular for VKH disease, birdshot retinochoroidopathy and Behçet's

disease (abstract, in particular the first and last sentences, and page 1490, right-hand column, first paragraph). Document D31a also confirmed this to be a model for autoimmune diseases (second paragraph).

Document D26 consisted of a chapter entitled "Autoimmune diseases of the eye" taken from a textbook on autoimmune diseases. Thus, when reading the document as a whole, any passages referring to "ocular inflammation" were to be read as referring to "autoimmune ocular inflammation". Part 6, which was entitled "Animal models for ocular autoimmune diseases", referred to the EAU-induced mouse model in the context of "ocular autoimmunity" and "human ocular inflammatory diseases" (page 986, right-hand column, first paragraph, third sentence from the end and second paragraph, penultimate sentence, respectively). Thus, this document disclosed EAU in mice as a model to study autoimmune diseases and not ocular inflammation in general. Moreover, the second of the passages above referred to Figure 2D, which was labelled as an image of the human eye, thus disclosing the link to human treatment.

Considerations relating to sufficiency of disclosure were of no relevance for the assessment of compliance with the requirements of Article 123(2) EPC. The above notwithstanding, according to the case law of the boards of appeal, experimental results obtained in animal models and even from *in vitro* experiments were accepted to demonstrate the suitability of a substance for therapy in humans.

Auxiliary request 1 - claim 1
Amendments - Article 123(2) EPC

Claim 1 of this request included the feature "*wherein said anti-IL-6 receptor antibody suppresses differentiation of CD4-positive T cells into TH17 cells*". This feature was found in paragraph [0087] of the application as filed. Paragraph [0088] referred to the treatment of humans. When read together, these two paragraphs disclosed the treatment of human autoimmune uveitis.

Auxiliary requests 2 to 5 - claim 1
Amendments - Article 123(2) EPC

No arguments specific to these requests were put forward.

XV. The appellant requested in writing that the decision under appeal be set aside and the patent be revoked. It further requested that documents D28 to D30 be admitted into the appeal proceedings.

The respondents requested that the appeal be dismissed (implying that the patent be maintained according to the claims found allowable by the opposition division and filed as the main request). Alternatively, they requested that the patent be maintained according to the claims of any of auxiliary requests 1 to 5, which were filed as auxiliary requests 5 and 1 to 4, respectively, with their reply to the statement of grounds of appeal. They further requested that documents D28 to D30 not be admitted into the appeal proceedings.

Reasons for the Decision

Admittance of documents D28 to D30 filed in appeal proceedings

1. The respondents requested that these documents, filed by the appellant, not be admitted into the appeal proceedings. The board did not take a decision on this issue since the decision does not rely on the content of these documents.

Main request - claim 1
Amendments - Article 123(2) EPC

2. Claim 1 defines a therapeutic application of an anti-IL-6 receptor antibody in the treatment of autoimmune uveitis.

3. It was common ground between the parties that, in the application as filed, there is no mention of "autoimmune uveitis" as such, and instead "experimental autoimmune uveitis" (EAU) is mentioned in relation to an animal model (EAU-induced mice).

4. It is established case law that any amendment to the patent application can only be made within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the description, claims and drawings of the application as filed (see decision G 2/10, OJ EPO 2012, 376, Reasons 4.3).

5. Determining the content of the application as filed requires in the case at hand an assessment of whether the disclosure of EAU-induced mice, when read by the

skilled person in the context of the whole application, directly and unambiguously discloses treatment of autoimmune uveitis.

6. Paragraph [0010] of the application as filed sets out the aim of the invention as the provision of therapeutic agents for ocular inflammatory diseases. Paragraph [0011] summarises the experimental findings on EAU-induced mice, and paragraph [0012] sets out the therapeutic applications of the findings. These three paragraphs read together convey to the skilled person that the experimental results in the application, obtained with the EAU-induced mice, are suitable to draw conclusions about a therapeutic effect of the anti-IL-6 receptor antibody on all diseases listed in paragraph [0012]. These include ocular inflammatory diseases in general, panuveitis, anterior uveitis, intermediate uveitis, scleritis, keratitis, orbital inflammation, optic neuritis, dry eye, diabetic retinopathy, proliferative vitreoretinopathy or postoperative inflammation (see items [1] and [5] of paragraph [0012]). Autoimmune diseases in general are not mentioned. None of the specific diseases classified according to document D26 as autoimmune uveitis is mentioned either.

7. The board concludes that, from an objective reading of the application as filed, the skilled person would not derive the use of anti-IL-6 receptor antibodies in general in the treatment of autoimmune uveitis.

8. In arriving at this conclusion, it is not of relevance that the terms "panuveitis" and "anterior uveitis" in paragraph [0012] refer to the location of the inflammation and thus do not exclude autoimmune

disease. Relevant is that autoimmune disease is not specified in this passage of the application as filed.

9. In the board's view, other passages referred to by the respondents are consistent with the above reading of paragraphs [0010] to [0012], as follows. Paragraph [0085] lists the same diseases as paragraph [0012]. Paragraph [0087] summarises the effect observed upon administration of the antibody to the EAU-induced mice.

10. The respondents argued that the application as filed discloses the treatment of autoimmune uveitis because it must be read using the common general knowledge of the skilled person. This included the knowledge that EAU-induced mice were an established model for autoimmune uveitis, as disclosed in documents D23, D26, D27 and D31a.

11. As concerns document D26, the board considers that it discloses EAU-induced mice as a model for a number of diseases including but not restricted to autoimmune uveitis, for the following reasons.

11.1 The respondents pointed to two passages in part 6 of this document, entitled "*Animal models for ocular autoimmune diseases*". These passages read:

"*Thus, EAU has become a stereotype of animal model for* ***ocular autoimmunity.***"

and

"*The various aspects of EAU therefore resemble a wide range of* ***human ocular inflammatory diseases affecting the retina and uvea*** *(Fig. 2D). Over the years, EAU has*

served as a model to elucidate basic mechanisms involved in pathogenesis and immune regulation of human uveitides and to develop new therapies for uveitic patients."

(See page 986, right-hand column, first and second paragraphs, respectively; emphasis by the board.)

11.2 From the quoted passages the board cannot conclude that EAU-induced mice were exclusively a model for autoimmune uveitis. Instead the board concludes that they were a model for inflammatory diseases affecting tissues such as the uvea and retina.

11.3 The respondents contested the view that document D26 disclosed EAU-induced mice as a model for ocular inflammatory diseases in general because it was exclusively concerned with autoimmune diseases. The board is not convinced by the respondents' argument that in this document "ocular inflammation" is to be read at every instance as "autoimmune ocular inflammation" and that, consequently, EAU-induced mice are disclosed as a model for autoimmune ocular diseases only. The document uses both expressions – "ocular autoimmune diseases" and "ocular inflammatory diseases" - and the board sees no reason to assume that they are not intentionally different. Thus, the board does not read the second of these two passages as relating specifically to autoimmune ocular inflammation.

11.4 Even when adopting the respondents' reading, the passages in question refer to "ocular autoimmune diseases" in general in which several tissues of the eye may be affected. Thus, the skilled person does not find in this document the information that EAU-induced mice are used exclusively to model autoimmune uveitis.

11.5 In fact, the information that the skilled person obtains from document D26 concerning the EAU-induced mouse model is thus no different from that in the application as a whole, according to which the EAU-induced mouse model was used to draw conclusions about therapeutic effects of relevance for a number of ocular diseases not restricted to autoimmune uveitis.

12. As concerns the disclosure in documents D23 and D27, the first refers to Vogt-Koyanagi-Harada (VKH) disease as an autoimmune disease, and the second discloses that EAU-induced mice are a model for the autoimmune diseases VKH disease, birdshot retinochoroidopathy and Behçet's disease. Document D31a refers to sympathetic ophthalmia and VKH disease and to the EAU-induced animal model. However, in the board's view, decisive is not whether EAU-induced mice were an established model for autoimmune uveitis but whether for the skilled person there was a univocal correspondence between this model and autoimmune uveitis. The board concludes that this was not the case, as stated in point 11.4 above.

13. In light of the above considerations, the board comes to the conclusion that the subject-matter of claim 1 of the main request extends beyond the content of the application as filed, contrary to the requirements of Article 123(2) EPC.

Auxiliary request 1 - claim 1
Amendments - Article 123(2) EPC

14. Apart from the deletion of the prophylactic use and the definition of the antibody as an inhibitor, claim 1 of auxiliary request 1 differs from claim 1 of the main request by the feature "*said anti-IL-6 receptor*

antibody suppresses differentiation of CD4-positive T cells into TH17 cells".

15. This feature is found in paragraph [0087] of the application.

16. The respondents argued that the skilled person would derive the treatment of human autoimmune uveitis from paragraph [0087] of the application, read in combination with the reference in paragraph [0088] to treatment of humans.

17. Paragraph [0087] summarises the experimental results obtained with EAU-IRBP-induced mice, stating that the degree of inflammation was reduced with the administration of an anti-IL-6 receptor antibody and that restimulation with the IRBP peptide resulted in a reduction in IL-17 secretion. From this the following is concluded at the end of the paragraph: "*Without being bound to a specific theory, the inventors of the present invention infer that the inhibitory effect of anti-IL-6 receptor antibody would be mediated by suppressed differentiation of CD4-positive T cells into TH 17 cells*."

18. Paragraph [0088] states that the "therapeutic agents for ocular inflammatory disease" are preferably to be administered to humans.

19. The board understands the respondents' argument to be that paragraph [0087] discloses that an effect on immune cells is involved in the therapeutic effect observed with administration of the antibody. However, the board considers that this passage does not provide any general disclosure that goes beyond observations on the animal model used in the experiments. Therefore,

inserting this feature into the claim does not overcome the issue of added mater regarding the feature "autoimmune uveitis" since this passage of the application also does not provide a general disclosure of the treatment of autoimmune uveitis.

20. The board comes to the conclusion that the subject-matter of claim 1 of auxiliary request 1 extends beyond the content of the application as filed, contrary to the requirements of Article 123(2) EPC.

Auxiliary requests 2 to 5 - claim 1
Amendments - Article 123(2) EPC

21. Claim 1 of each request defines a therapeutic application in the treatment of autoimmune uveitis, with claim 1 of auxiliary requests 2 and 4 including the feature addressed above in the context of auxiliary request 1.

22. Thus, the reasons given under points 14. to 19. apply to claim 1 of auxiliary requests 2 and 4, and those given under points 2. to 12. apply to claim 1 of auxiliary requests 3 and 5. Accordingly, the subject-matter of claim 1 of auxiliary requests 2 to 5 extends beyond the content of the application as filed, contrary to the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated