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Datasheet for the decision of 19 November 2014

Case Number: T 2273/09 - 3.3.02

Application Number: 99909307.3

Publication Number: 1072273

IPC: A61K45/00

Language of the proceedings: EN

Title of invention:
VASCULARIZATION INHIBITORS

Patent Proprietors:
CHUGAI SEIYAKU KABUSHIKI KAISHA
Kishimoto, Tadamitsu

Opponents:
ELI LILLY AND COMPANY
STRAWMAN LIMITED

Headword:
CXCR4 inhibition for inhibiting vascularization/CHUGAI

Relevant legal provisions:
EPC Art. 123(2), 112

Keyword:
Amendments - added subject-matter (yes)
Referral to the Enlarged Board of Appeal (no)

Decisions cited:
T 0727/00, T 1374/07, T 0783/09, G 0002/10, G 0003/89, G 0011/91

Catchword:
./.

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Case Number: T 2273/09 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 19 November 2014

Appellant: (Patent Proprietor 1)	CHUGAI SEIYAKU KABUSHIKI KAISHA 5-1, Ukima 5-chome, Kita-ku Tokyo, 115-8543 (JP)
Appellant: (Patent Proprietor 2)	Kishimoto, Tadamitsu 3-5-31, Nakano-cho Tondabayashi-shi, Osaka 584-0021 (JP)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Respondent: (Opponent 1)	ELI LILLY AND COMPANY Lilly Corporate Center Indianapolis IN 46285 (US)
Representative:	Burnside, Ivan John Eli Lilly and Company Limited Lilly Research Centre Erl Wood Manor Sunninghill Road Windlesham Surrey GU20 6PH (GB)
Respondent: (Opponent 2)	STRAWMAN LIMITED 34 Lovedon Lane Winchester, Hampshire, SO23 7NU (GB)
Representative:	Walton, Seán Malcolm Mewburn Ellis LLP 33 Gutter Lane London EC2V 8AS (GB)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 3 November 2009 revoking European patent No. 1072273 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman U. Oswald
Members: H. Kellner
L. Bühler

Summary of Facts and Submissions

I. European patent No. 1 072 273 with application No. 99 909 307.3, based on international application PCT/JP1999/001448 published as WO 1999/048528, was granted with sixteen claims.

Independent claims 1 to 3 as granted read as follows:

"1. Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament **for inhibiting vascularization**, wherein the substance is selected from the group consisting of
(1) a substance inhibiting the binding between SDF-1 and CXCR4;
(2) a substance inhibiting the signaling from CXCR4 to nuclei;
(3) a substance inhibiting the expression of CXCR4; and
(4) a substance inhibiting the expression of SDF-1.

2. Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament **for a solid cancer**, wherein the substance is selected from the group consisting of
(1) a substance inhibiting the binding between SDF-1 and CXCR4;
(2) a substance inhibiting the signaling from CXCR4 to nuclei;
(3) a substance inhibiting the expression of CXCR4; and
(4) a substance inhibiting the expression of SDF-1.

3. Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament **for inhibiting a disease pathologically caused by neovascularization**, wherein the substance is selected from the group consisting of

(1) a substance inhibiting the binding between SDF-1 and CXCR4;
(2) a substance inhibiting the signaling from CXCR4 to nuclei;
(3) a substance inhibiting the expression of CXCR4; and
(4) a substance inhibiting the expression of SDF-1."
(words in bold and formatting by the board)

II. Opposition was filed against the granted patent under Article 100(a) EPC, on the grounds of lack of novelty and lack of inventive step and under Article 100(b) EPC for insufficiency of disclosure.

III. By its decision pronounced at oral proceedings on 30 September 2009 and posted on 3 November 2009, the opposition division revoked the patent under Article 101(3)(b) EPC.

The opposition division held that the patent according to the main request and first auxiliary request did not meet the requirements of Article 123(2) EPC. The subject-matter of the second auxiliary request, filed and amended at the oral proceedings before the opposition division, was found not inventive under Articles 100(a) and 56 EPC.

IV. The patent proprietors (appellants) lodged an appeal against that decision.

With their statement of grounds of appeal, the appellants filed three sets of claims as their main request and first and second auxiliary request.

The main request is identical to the second auxiliary request decided on by the opposition division.

With respect to the claims as granted, the independent use-claims 1 to 3 of the main request differ from claims 1 to 3 in the published patent in that the features
"(2) a substance inhibiting the signaling from CXCR4 to nuclei" and
"(3) a substance inhibiting the expression of CXCR4" have been deleted and original feature (4) is now number (2):

"1. Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament **for inhibiting vascularization**, wherein the substance is selected from the group consisting of
(1) a substance inhibiting the binding between SDF-1 and CXCR4; and
(2) a substance inhibiting the expression of SDF-1.

2. Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament **for a solid cancer**, wherein the substance is selected from the group consisting of
(1) a substance inhibiting the binding between SDF-1 and CXCR4; and
(2) a substance inhibiting the expression of SDF-1.

3. Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament **for inhibiting a disease pathologically caused by neovascularization**, wherein the substance is selected from the group consisting of
(1) a substance inhibiting the binding between SDF-1 and CXCR4; and
(2) a substance inhibiting the expression of SDF-1."
(words in bold and formatting by the board)

The wording of the single independent claim of the first auxiliary request is:

"Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament for a solid cancer, wherein the substance is a substance inhibiting the binding between SDF-1 and CXCR4."

The single claim of the second auxiliary request is:

"Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament for a solid cancer,
wherein the substance is a substance inhibiting the binding between SDF1 and CXCR4,
wherein the substance inhibits CXCR4,
wherein the substance inhibits SDF-1 from binding to CXCR4 by binding to CXCR4, and
wherein the substance is one selected from the group consisting of an anti-CXCR4 antibody, a fragment of said antibody possessing the activity of anti-CXCR4 antibody and a fused protein possessing binding activity to CXCR4."

V. The board sent a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) as an annex to the summons to oral proceedings.

With its communication the board expressed in particular concern that the sets of claims of the main and first and second auxiliary requests appeared to contain amendments extending beyond the content of the application as filed. Moreover, the board indicated that the single claim of the second auxiliary request

appeared to unallowably broaden the scope of the patent as granted (Article 123(3) EPC).

VI. With letter of 7 October 2014 the appellants submitted third and fourth auxiliary requests.

The subject-matter of the third auxiliary request differs from the main request filed with the grounds of appeal in that dependent claims 4 to 15 have been amended. Independent claims 1 to 3 remain unchanged.

The single claim of the fourth auxiliary request relates to the second auxiliary request and reads as follows:

"Use of a substance that inhibits the action due to CXCR4 in the manufacture of a medicament for a solid cancer, wherein
1) the substance is a substance inhibiting the binding between SDF1 and CXCR4,
2) the substance of 1) inhibits CXCR4,
3) the substance of 2) inhibits SDF-1 from binding to CXCR4 by binding to CXCR4, and
4) the substance of 3) is one selected from the group consisting of
an anti-CXCR4 antibody,
a fragment of said antibody possessing the activity of anti-CXCR4 antibody and
a fused protein possessing binding activity to CXCR4."

VII. Oral proceedings took place on 19 November 2014 before the board. Duly summoned, respondent-opponents 1 and 2 had informed the board in advance that they would not be attending.

During the oral proceedings, the appellants filed a request pursuant to Article 112 EPC that the following two questions, being interconnected and relating to the same issue, be referred to the Enlarged Board of Appeal:

"1) When is the deletion of several members from two lists, wherein all combinations are described as equally preferred, violating Article 123(2) EPC? (with reference to T 783/09 and T 727/00)

2) If the answer to question 1) above is that such a selection is never allowable: when is a deletion of several members of one list, all members of which are described as equally preferred, violating Article 123(2) EPC? (with reference to T 1374/07)"

This request and the claim requests were discussed *inter alia* in the light of the decision of the Enlarged Board of Appeal G 2/10 (OJ EPO 2012, 376).

VIII. The appellants' submissions as far as relevant to this decision may be summarised as follows:

The subject-matter of each of the three independent claims of the main request should be assessed separately.

The separate therapeutic aspects of these claims were reflected at several parts of the application as originally filed, for instance on page 1, lines 4 to 8 and in independent claims 1 to 3 (see English version of the application filed with the EPO on 12 October 2000). These therapeutic aspects were linked by the underlying concept of the CXCR4 inhibition as disclosed on page 6, lines 18 to 21 and supported by

the example of the knock-out mouse model, which represented a predictive model used in the technical field. Based on this model, the person skilled in the art would consider the independent therapeutic aspects of the application as filed as equally predictive.

As an agent for use in these therapeutic aspects, the application as originally filed disclosed "a substance that inhibits the action due to CXCR4", specifically mentioning four groups of substances as defined on page 16, lines 11 to 22 and reflected in dependent claims 5 to 8.

The application as originally filed therefore directly and unambiguously disclosed 16 individual combinations of independent claims 1 to 4 with each of dependent claims 5 to 8. As the application did not describe any of the therapeutic aspects or any of the four inhibitor types (groups of substances) as more preferred than the others, these combinations were to be considered as equally preferred.

In view of decision T 783/09, finding that claiming three of forty-four combinations of the "same quality" did not unallowably extend the content of the application as filed, the subject-matter of the current requests, which likewise did not result from a selection but only from the deletion of ten or fifteen from the sixteen individual combinations directly and unambiguously disclosed, fulfilled the requirements of Article 123(2) EPC.

If the board came to a conclusion differing from decision T 783/09, the referral of the proposed questions to the Enlarged Board of Appeal pursuant to

Article 112 EPC (see point VII. above) should be allowed.

IX. The respondents did not provide any written arguments with respect to Article 123(2) EPC.

X. The appellants (patent proprietors) requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request, or, alternatively, of one of the first or second auxiliary request, all filed with the statement of grounds of appeal, or of one of the third or fourth auxiliary request filed with letter dated 7 October 2014. Moreover, the appellants requested that two questions be referred to the Enlarged Board of Appeal.

XI. The respondents (opponents) had requested in writing that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. Article 123(2) EPC

2.1 Main request

2.1.1 The **application as originally filed** (see English version of the application filed with the EPO on 12 October 2000) contained independent claims 1 to 4, relating to
(1) a therapeutic agent for inhibiting vascularisation
(2) a therapeutic agent for solid cancer
(3) a therapeutic agent for a disease pathologically caused by neovascularisation and

(4) a therapeutic agent for repairing a tissue.

The therapeutic applications contained in these four independent claims are reflected in several parts of the description, for instance page 1, lines 4 to 11; page 4, line 25 to page 5, line 13; page 5, line 23 to page 6, line 10 or page 14, lines 14 to 22. None of these therapeutic applications is characterised as specifically advantageous in the application as originally filed.

The effective ingredient "for" the therapeutic applications is defined in the original claims 1 to 4 as "a substance that inhibits the action due to CXCR4", referred to in the remainder of this decision as "CXCR4 "inhibiting substance"".

Claims 5 to 8 as originally filed, each of which is dependent on claims 1 to 4, further define "a substance that inhibits the action due to CXCR4" (CXCR4 "inhibiting substance") as
(5) a substance inhibiting the binding between SDF-1 and CXCR4;
(6) a substance inhibiting the signaling from CXCR4 to nuclei;
(7) a substance inhibiting the expression of CXCR4; and
(8) a substance inhibiting the expression of SDF-1.

The four different classes of CXCR4 "inhibiting substances" according to these four claims are also reflected in the description of the application as originally filed, especially on page 16, lines 16 to 22. None of these four general classes of CXCR4 "inhibiting substances" is disclosed as specifically advantageous.

2.1.2 In Swiss-type claims, like those of the **patent in suit**, the therapeutic use is a functional technical feature which may confer novelty and inventive step and which is thus linked to the claimed use of an effective ingredient for the manufacture of a medicament. On this basis, original dependent claims 5 to 8 define four classes of CXCR4 "inhibiting substances", which, in the patent **as granted**, are combined as effective ingredients with three of the four independent therapeutic applications. In fact, in each of the independent claims 1 to 3 **as granted**, one therapeutic application is combined with all four classes of CXCR4 "inhibiting substances". However, each therapeutic application might also be combined with each class of CXCR4 "inhibiting substances" separately or in groups of two or three.

2.1.3 To summarise, the **application as originally filed** relates to a plurality of possible combinations, which result from combining the subject-matter of independent claims 1 to 4 relating to four therapeutic applications, with the subject-matter of one or more of dependent claims 5 to 8 disclosing four different classes of the CXCR4 "inhibiting substances".

However, none of the plurality of possible combinations of a therapeutic application with a class of active substances is explicitly mentioned in the application as originally filed, in particular not in the form of a Swiss-type second medical use claim. Consequently, none of these combinations can be regarded as individualised in the application as filed and, therefore, none of them is originally disclosed as such.

2.1.4 The set of claims of the **main request** contains three independent use claims in the Swiss-type form.

The teaching of these claims relates to the three therapeutic applications mentioned in claims 1 to 3 as originally filed, in combination with the two classes of CXCR4 "inhibiting substances" as defined in dependent claims 5 and 8 as originally filed, thus representing six specific combinations.

As none of the plurality of the possible specific combinations in the application as a whole is either explicitly mentioned or individualised in any other way in the application as originally filed (see point 2.1.3 above), this group of six of the possible combinations is also not explicitly mentioned or exemplified (neither the specific combinations being present in this group of six nor the particular number of six).

In addition, no information was originally provided that, as subject-matter to be claimed, the precise three therapeutic applications mentioned in claims 1 to 3 as originally filed were to be combined in a Swiss-type claim with the two classes of CXCR4 "inhibiting substances" as defined in dependent claims 5 and 8 as originally filed.

2.1.5 Decision G 2/10 (OJ EPO 2012, 376) refers to "the general definition of the requirements of Article 123(2) EPC established in opinion G 3/89 and decision G 11/91, which definition has become the generally accepted, one could also say the "gold" standard, for assessing any amendment for its compliance with Article 123(2) EPC" (bottom of page 30). According to the first full paragraph on page 27 of G 2/10, this statement includes an assessment of the *ratio decidendi* of decisions G 1/93

(OJ EPO 1994, 541, answer 1, first sentence) and G 2/98 (OJ EPO 2001, 413).

The first two paragraphs of point 4.5.4 of decision G 2/10 (page 39) state that in order to assess the requirements of Article 123(2) EPC, in the case of disclosed disclaimers as well as in the case of limiting a claim by a positively defined feature (as with the claims in suit), there is a need to technically assess the case under consideration and to answer the question, whether the skilled person, using common general knowledge, would regard the remaining subject-matter claimed as **explicitly or implicitly**, but directly and unambiguously, disclosed in the application as filed.

The focus on the remaining subject-matter claimed is particularly relevant with respect to the appellants' declaration that the subject-matter of the current requests did not result from a selection but only from the deletion of some individual combinations from "the sixteen" directly and unambiguously disclosed (see point VIII. above, last three paragraphs).

2.1.6 According to points 2.1.1 to 2.1.4 above, the application as originally filed does not contain an **explicit** disclosure of the remaining claimed subject-matter of the main request.

2.1.7 It follows that it must be assessed if the remaining group of six combinations as claimed with the main request is implicitly disclosed in the application as originally filed.

The assessment of the overall technical circumstances of the current case in the light of the first two

paragraphs of point 4.5.4 of decision G 2/10 reveals that the six combinations of the independent claims of the main request can in principle result from the original application

either by

(a) virtually combining all four disclosed individual therapeutic applications with all four of the classes of effective ingredients in groups of one, two, three or four to form the overall maximum possible number of combinations and

building the final number of six combinations by reducing the overall number of combinations by abandoning the rest of the combinations (as the appellants suggested) or

(b) selecting from these multiple combinations the number of six claimed combinations

or by

(c) selecting three from the full list of four therapeutic applications or reducing this full list of therapeutic applications by one and selecting two from the full list of four classes of effective ingredients or reducing this full list of classes of effective ingredients by two and

combining the remaining three and two individual ones respectively.

Once again it has to be emphasised that none of the combinations contained in the maximum number of combinations is either explicitly mentioned or in any

other way individualised in the application as originally filed.

Even ignoring this basic problem, in order to arrive at the subject-matter of the main request and in assessing whether this remaining group of six combinations is directly and unambiguously disclosed,

(a) starting from the overall maximum possible number of combinations it would be necessary to know exactly how many and which combinations have to be deducted from this overall maximum possible number. Nothing, however, is disclosed about that in the application as originally filed or is known from common general knowledge.

(b) On the other hand, just selecting the claimed six specific combinations out of all possible combinations is also impossible on the basis of the disclosure as originally filed, because to do that the skilled person would have to know beforehand that he should select exactly the number of six out of the possible combinations and which of the overall possible combinations should be contained in the resulting group.

(c) The assessment of the other possible ways of arriving at the subject-matter as claimed reveals that therapeutic agents for four different therapeutic applications, mentioned in independent claims 1 to 4 of the application as filed, are presented as embodiments of equal quality. The skilled person therefore finds no disclosure or indication in the application as filed for selecting one or more particular ones of the four equally presented therapeutic applications or for

restricting himself to one or more of them. He would also not be prompted by his common general knowledge to make such a selection or restriction.

The four different classes of the CXCR4 "inhibiting substances" are also presented as classes of effective ingredients of the invention of equal quality. None of the classes of the CXCR4 "inhibiting substances" is characterised as being advantageous compared to the other classes and there is also no technical teaching to be found in the application as filed or by using common general knowledge that could lead the person skilled in the art to consider one or more of the four classes as particular. The person skilled in the art therefore finds no disclosure or indication for selecting the specific two classes of CXCR4 "inhibiting substances" as claimed in the main request or for restricting to the two claimed ones the four classes of CXCR4 "inhibiting substances" originally presented as equal.

2.1.8 Furthermore, the sole example of the application relates to a knock-out model of mice lacking the complete CXCR4 gene used to determine the physiological function of CXCR4. The board does not deny that this is a predictive model used in the technical field. However, the model neither uses a particular one of any of the four different classes of CXCR4 "inhibiting substances" nor is it specifically linked to one of the four therapeutic applications. Thus, the example of the application as originally filed likewise fails to disclose or indicate to the person skilled in the art that one or more of the four therapeutic applications or one or more of the classes of CXCR4 "inhibiting substances" is more relevant than the others.

Moreover, in the absence of any specific information in the example relating to a particular therapeutic application or a specific CXCR4 "inhibiting substance", there is also no possibility to derive the subject-matter of claims 1 to 3 of the main request by means of a *lege artis* allowable intermediate generalisation linking the general teaching of the application as filed to information extracted from the example.

2.1.9 From these considerations it is clear that the skilled person is not prompted by any particular emphasis on the elements that are combined in one or all of independent claims 1 to 3 of the main request to find the resulting combinations **implicitly** disclosed.

2.1.10 Taken together, the specific number of possible combinations contained in claims 1 to 3 of the main request is not exemplified in the application as originally filed, expressed in the sole example, or disclosed in the application as originally filed as specifically derivable in a direct and unambiguous way.

It is therefore concluded that the application as originally filed neither explicitly nor implicitly discloses the subject-matter of the main request.

2.1.11 The appellants' argument relating to separate assessment of each of the independent claims of the main request

The same arguments apply *mutatis mutandis* to each of the three independent claims of the main request alone, as their subject-matter relates to a number of combinations in the form of a combination of one of the

therapeutic applications with two CXCR4 "inhibiting substances".

Considering each of these claims alone and trying to derive it directly and unambiguously from its single counterpart in the application as filed without regard to the other independent claims as originally filed, and in that way disregarding the content of the original application as a whole, is contrary to the provisions of Article 123(2) EPC.

For assessing whether the application contains subject-matter which extends beyond the original content, this article relates to the application as a whole and not to isolated parts of it (see also point 4.3 beginning on page 26 of decision G 2/10, first paragraph).

2.1.12 The appellants' arguments relating to decision T 783/09 of 25 January 2011 (not published in the Official Journal)

The board in T 783/09 concluded that, for a therapeutic composition containing two active ingredients, based on the disclosure of two individual DPP-IV inhibitors for the first ingredient and twenty-two individual antidiabetic compounds for the second ingredient, the skilled person would directly and unambiguously recognise forty-four individual combinations of ingredients. Deleting some of these "individualised" combinations from this list of equally preferred elements was not in breach of Article 123(2) EPC.

In the appellants' opinion, the same reasoning and conclusion applied to the subject-matter of the main request in the current case relating to the deletion of ten of sixteen directly and unambiguously disclosed

individual combinations, with six combinations then remaining.

In decision G 2/10, issued after T 783/09, namely on 30 August 2011, it is however stated that

"Whether the skilled person is presented with new information depends on how he or she would understand the amended claim, i.e. the subject-matter ***remaining in the amended claim*** *and on whether, using common general knowledge, he or she would regard that subject-matter as at least implicitly disclosed in the application as filed.*
That statement corresponds to the definition given in Article 123(2) EPC" (see page 37, second and third paragraph; emphasis by the board).

and

"Also, no so-called rule of logic applies, in the sense that where an application discloses a general teaching and specific embodiments, groups thereof or areas, all other potential embodiments or intermediate generalisations falling within the ambit of the general teaching (but not as such disclosed in the application as filed) would thereby, by implication, inevitably also be disclosed" (see page 39, first paragraph).

The conclusion drawn from the situation given in decision G 2/10 is the necessity of the technical assessment of the case under consideration with regard to the remaining subject-matter claimed, as performed for the current case under points 2.1.1 to 2.1.10 above.

2.1.13 Thus, applying the EPC in line with the more recent Enlarged Board of Appeal decision G 2/10, it is found that the subject-matter of the main request under consideration in this decision does not meet the requirements of Article 123(2) EPC.

2.2 Auxiliary requests

2.2.1 The teaching of the independent claims of the first, second and fourth auxiliary requests is further restricted with respect to the number of selected combinations in comparison with the teaching of the main request.

As the teaching of the independent claims of these requests is also not individualised in the application as originally filed, no explicit direct and unambiguous disclosure can be acknowledged. Concerning an implicit but direct and unambiguous disclosure of that teaching, the arguments set out under points 2.1.1 to 2.1.10 above apply *mutatis mutandis*.

2.2.2 The teaching of independent claims 1 to 3 of the third auxiliary request is identical to the main request. The arguments set out under point 2.1 above therefore again apply.

2.2.3 Consequently, it is found that the teaching of the auxiliary requests is in breach of Article 123(2) EPC.

3. Request for referral to the Enlarged Board of Appeal under Article 112 EPC

The board in its present decision has taken due account of the Enlarged Board of Appeal's decision G 2/10, published on 30 August 2011, i.e. after the issue of

T 783/09. In particular, the need for a technical assessment of the case under consideration with regard to the remaining subject-matter claimed was discussed under point 2.1 above. The more recent decision G 2/10 being valid, the board cannot agree with the appellants' argument that - in the relevant aspects - there is divergent case law of the boards of appeal.

In addition, the two questions as filed are answered by the considerations and conclusions of decision G 2/10 as cited in this decision. Consequently, the request for their further referral must be refused.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

2. The request for referral to the Enlarged Board of Appeal is refused.

The Registrar: The Chairman:

N. Maslin U. Oswald

Decision electronically authenticated