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Datasheet for the decision of 25 September 2013

Case Number: T 0400/11 - 3.3.01

Application Number: 04005836.4

Publication Number: 1426361

IPC: C07D221/04, A61K31/352, A61K47/12, A61P11/08

Language of the proceedings: EN

Title of invention:
Novel composition containing a bi-cyclic compound and a glyceride

Patent Proprietor:
Sucampo AG

Opponent:
Johnson Matthey PLC

Headword:
Tautomers/SUCAMPO

Relevant legal provisions:
EPC Art. 54, 87, 114(2)
RPBA Art. 13(1)

Keyword:
Late-filed evidence - admitted (no)
Novelty - all requests (no)

Decisions cited:

Catchword:

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Case Number: T 0400/11 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 25 September 2013

Appellant: (Patent Proprietor)	Sucampo AG Graben 5 6300 Zug (CH)
Representative:	Albrecht, Thomas Kraus & Weisert Patent- und Rechtsanwälte Thomas-Wimmer-Ring 15 80539 München (DE)
Respondent: (Opponent)	Johnson Matthey PLC 40-42 Hatton Garden London EC1N 8EE (GB)
Representative:	Whitcombe, Nicole Jane Johnson Matthey PLC Gate 20 Orchard Road Royston Hertfordshire SG8 5HE (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 14 December 2010 concerning maintenance of the European Patent No. 1426361 in amended form.**

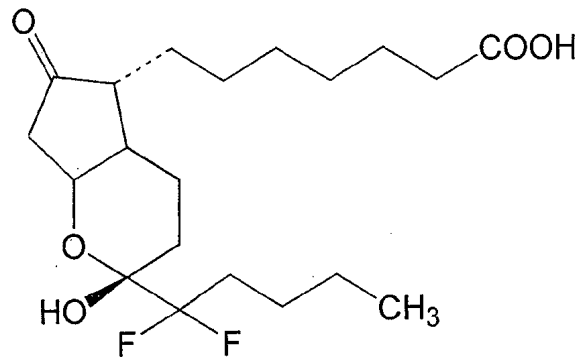
Composition of the Board:

Chairman:	A. Lindner
Members:	L. Seymour
	L. Bühler

Summary of Facts and Submissions

I. The appeal lies from the interlocutory decision of the opposition division maintaining the European patent No. 1 426 361 in amended form, on the basis of auxiliary request 5 filed at oral proceedings before the opposition division. Claim 1 of this request reads as follows:

"1. A pharmaceutical composition comprising a bi—cyclic compound represented by the formula



7-[(1R,3R,6R,7R)-3-(1,1-difluoropentyl)-3-hydroxy-2-oxabicyclo[4.3.0]nonane-8-one-7-yl]heptanoic acid and its salt, ether, ester or amide thereof, wherein the ratio of bi-cyclic tautomer to mono-cyclic tautomer is 100:0."

Note: for the sake of conciseness, the compound identified above is referred to herein as "compound 1" (cf. also patent in suit, paragraphs [0040] and [0041]).

II. Reference is made below to the following documents cited during the opposition/appeal proceedings:

(3) EP-A-0 430 551

(6) English translation of present priority application US 60/159,549

(8) WO 02/20007

(9) US 09/655,760 (priority application of document (8))

(10) EP-A-0 345 951

III. The patentee filed an appeal against the decision of the opposition division, and submitted six auxiliary requests with its statement of grounds of appeal.

IV. The respondent (opponent), who had opposed the patent in suit under Articles 100(c), 100(b) and 100(a) EPC (lack of novelty and inventive step), took no part in the appeal proceedings. A second opponent withdrew its opposition during opposition proceedings.

V. In a communication dated 20 June 2013 sent as annex to the summons to oral proceedings, attention was drawn to certain issues arising under Articles 123(2), 84 and 54 EPC. It was further noted that sufficiency of disclosure may have to be discussed.

VI. With letter dated 23 August 2013, the appellant filed a main request and three auxiliary requests to replace the requests previously on file.

Claim 3 of the main request differs from claim 1 reproduced above in point I in the replacement of the expression "wherein the ratio of bi-cyclic tautomer to

mono-cyclic tautomer is 100:0" with "wherein the composition is substantially free of water".

Claim 7 of the main request differs from claim 1 reproduced above in point I in the insertion of "substantially" in front of the ratio "100:0".

Claim 3 of the main request is also present as claim 1 in auxiliary request 2, and claim 7 of the main request as claim 1 in auxiliary request 3.

Auxiliary request 1 filed with letter dated 23 August 2013 was subsequently modified during oral proceedings (see point VII below).

VII. Oral proceedings were held before the board on 25 September 2013.

During the course of the oral proceedings, the appellant replaced its previous auxiliary request 1 with a new auxiliary request 1 dated 25 September 2013. Claim 3 of this request is identical to claim 7 of the main request (see preceding point VI).

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

The evidence filed on 20 September 2013 provided confirmation for the fact that the 100% bicyclic tautomer could be obtained for compound 1 in crystalline form. It should be admitted into the proceedings since it had been submitted in response to the board's communication, and specifically the reference therein to possible problems of sufficiency of disclosure. It also might be of relevance for the analysis of novelty.

The basis in the application as originally filed for the feature "wherein the composition is substantially free of water", present in claim 3 of the main request, was to be found on page 32, lines 24 and 25. In claim 7 of the main request, the feature "wherein the ratio of bi-cyclic tautomer to monocyclic tautomer is substantially 100:0" was based on the expression "substantially all bi-cyclic compound" found in the sentence disclosed in application as originally filed on page 12, lines 2 to 7.

As regards the issue of novelty of the main request, the appellant generally submitted that the subject-matter claimed was based on the surprising discovery, as described in paragraph [0039] of the patent in suit, that in the absence of water, compound 1 existed substantially 100% in its bicyclic form. This teaching had not been made available to the public prior to the filing date of the opposed patent. The prior art, such as document (3), only disclosed equilibrium mixtures of monocyclic and bicyclic tautomers. In contrast, the patent in suit disclosed compound 1 in crystalline form, as shown in Table 1 (paragraph [0085]). Said crystal consisting of 100% bicyclic compound was not disclosed in the prior art.

Turning to claim 3 of the main request, the appellant denied that the lyophilised powder according to Formulation Example 7 of document (3) fell within its scope. Claim 3 was to be construed in the light of the description of the patent in suit; the skilled person would understand from paragraph [0039] that the feature "substantially free of water" implied that the compound was solely present in bicyclic form. In contrast, in Formulation Example 7 of document (3), water had been

added to the mixture prior to lyophilisation. Therefore, the powder obtained would contain a mixture of the mono- and bicyclic forms.

With respect to claim 7 of the main request, the appellant submitted that document (8) was not available as state of the art under Article 54(3) EPC, since the patent in suit was entitled to the claimed priority date based on document (6). Moreover, even if only partial priority were to be acknowledged for the patent in suit, document (8) would nevertheless not anticipate the subject-matter of claim 7, since it did not make available 100% bicyclic compounds or compositions thereof, and, in particular, did not disclose how the latter were to be obtained, namely, by crystallisation.

The reasoning presented for the main request applied equally to the corresponding claims of the auxiliary requests.

IX. The appellant (patent proprietor) requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request filed with letter of 23 August 2013, or, alternatively, on the basis of auxiliary request 1 filed during oral proceedings of 25 September 2013, or alternatively, on the basis of one of auxiliary requests 2 and 3 filed with letter of 23 August 2013.

X. At the end of the oral proceedings, the decision of the board was announced.

Reasons for the Decision

1. The appeal is admissible.

2. *Admissibility of requests*

In the main request and auxiliary requests 2 and 3 filed with the letter of 23 August 2013, the amendments undertaken with respect to auxiliary requests filed with the statement of grounds of appeal were of a clear and simple nature. Moreover, said requests were filed as a direct response to the communication sent as annex to the invitation to oral proceedings (cf. above point V).

Similarly, in auxiliary request 1 filed during oral proceedings before the board, the amendments merely consisted in the deletion of two independent claims present in the main request.

The board therefore decided to exercise its discretion to admit these requests into the proceedings (Article 13(1) of the Rules of Procedure of the Boards of Appeal (RPBA); see Supplement to OJ EPO 1/2013, pages 38 to 49).

3. *Admission of evidence filed on 20 September 2013*

This evidence was filed only a few days prior to oral proceedings before the board. As with all late-filed evidence, admissibility is a matter for the discretion of the board, in accordance with Article 114(2) EPC and Article 13(1),(3) RPBA. In this context, account may *inter alia* be taken of whether a convincing case has been made as to why the evidence could not have been filed earlier and as to its *prima facie* relevance.

The appellant justified the filing of this evidence as being in response to the board's communication of 20 June 2013. However, sufficiency of disclosure and novelty were already an issue during the opposition proceedings (cf. above point IV). Indeed, in the reply to the notices of opposition dated 28 January 2010 (page 9, penultimate paragraph), the following was stated in relation to the issue of sufficiency of disclosure (emphasis added):

"In claims 1 to 4, the compounds per se are claimed. These claims are supported, inter alia, by paragraph [0085] of the opposed patent relating to **crystalline forms of compounds 1 and 2 that were prepared and confirmed to be 100% bi-cyclic compounds.**"

In view of the fact that this statement was made in 2010 and in view of the fact that the declaration of Mr Ryuji Ueno is dated 4 August 2011, it is apparent that the evidence in question had been available at least two years prior to its filing. Therefore, if considered necessary, it could and should have been submitted at a much earlier stage of the proceedings.

Furthermore, it is not considered that the appellant has made a convincing case as to the relevance of the data filed. In the patent in suit, the term "crystal" only appears in Table 1, in the context of providing control samples in stability tests on storage (see paragraphs [0077] and [0085]), and no information is provided as to how the crystals were obtained. Moreover, crystallinity is not disclosed in the context of measures to be taken in order to obtain compounds exclusively in its bicyclic form (cf. paragraph [0039]). This feature is also not present in any of the

claims under consideration. Therefore, the board is not convinced that the late-filed data, pertaining to a single crystal form of compound 1, of unspecified origin, could be seen as being relevant to any potential discussion with respect to sufficiency of disclosure or novelty.

Consequently, the board decided not to admit this evidence into the proceedings (Article 114(2) EPC, Article 13(1),(3) RPBA).

4. In view of the outcome of these appeal proceedings on the question of novelty (see points 5 and 6 below), it is not necessary to discuss the question of formal allowability of the main request and of auxiliary requests 1 to 3 (Articles 123 and 84 EPC), or sufficiency of disclosure (Articles 100(b), 83 EPC).

5. Main request, novelty

5.1 The analysis below focuses on an examination of the novelty of independent claims 3 and 7 with respect to documents (3) and (8), respectively.

5.2 Claim 3 of the main request relates to a pharmaceutical composition comprising compound 1, "wherein the composition is substantially free of water".

5.2.1 Document (3) discloses, on page 16, lines 4 to 39, the 15-ketoprostaglandin compound (39') (16,16-difluoro-13,14-dihydro-15-keto-PGE_1), which is the monocyclic tautomer of present compound 1 (see also document (3), formula on page 13, lines 23 to 30, R = H).

It is further disclosed in document (3) that the keto (monocyclic) and hemiacetal (bicyclic) forms are in equilibrium, that the proportion of tautomeric isomers will depend on the structure of the molecule, and that the compounds used in the invention include both isomers (see page 5, lines 32 to 41).

Pharmaceutical compositions are listed in document (3) on page 13, line 42 to page 14, line 16. A specific example thereof is disclosed in Formulation Example 7 (page 18, lines 9 to 21). In this example, compound (39'), mannitol and distilled water were mixed, stirred, sterilized, filtered and lyophilised to give powders for injection. Lyophilisation is a dehydration process, and the resulting powders are therefore "substantially free of water".

Moreover, since electron-withdrawing group, such as fluorine, at position 16 of the present types of structure are known to favour the bicyclic tautomer (see document (10), page 5, lines 11, 12 and page 6, lines 4 to 6; and patent in suit, paragraph [0039], which is reproduced below), it is safe to conclude that a portion of compound (39') in the the lyophilised powder is in the form of the bicyclic tautomer. This was not disputed by the appellant

5.2.2 However, the appellant submitted that the subject-matter of present claim 3 was nevertheless novel with respect to the powder according to Formulation Example 7, since the former was to be construed in the light of the description of the patent in suit as relating to compositions comprising solely the bicyclic form. Therefore, a composition comprising mixtures of tautomers, such as that disclosed in document (3), would not fall within its scope.

This argument is not considered to be persuasive. In the relevant passage of the patent in suit, the following is stated (paragraph [0039], emphasis added):

"However, it has been discovered that in the absence of water, the tautomeric **compounds** as above exist **predominantly** in the form of the **bi-cyclic compound**. In aqueous media, it is believed that hydrogen bonding occurs between the water molecule and, for example, the keto group at the hydrocarbon chain, thereby hindering bicyclic ring formation. In addition, it is believed that the halogen atom(s) at X_1 and/or X_2 promote bi-cyclic ring formation, such as the compound 1 or 2 below. The bi-cyclic/mono-cyclic structures, for example, may be present in a ratio of 6:1 in D_2O; 10:1 in CD_3OD-D_2O and 96:4 in $CDCl_3$. Accordingly, a preferable embodiment of the present invention is the **composition** in which the bi-cyclic form is present in ratio of bi-cyclic/mono-cyclic of at least **50:50**, preferably **90:10**, or even greater to **substantially all** bi-cyclic compound; **100% bi-cyclic compound** is within this invention."

It can be seen from the above paragraph that a distinction is made between compounds and compositions, and that, with respect to the compositions, various mixtures of tautomers are envisaged as preferred embodiments. Therefore, contrary to the appellant's contention, it cannot be accepted that claim 3 is to be construed as being in any way restricted with respect to the ratio of tautomers present.

5.2.3 In view of the above, it is concluded that the powder according to Formulation Example 7 of document (3) possesses all the features defined in claim 3. The

subject-matter of this claim therefore lacks novelty within the meaning of Articles 52(1) and 54(2) EPC.

5.3 Claim 7 of the main request relates to a pharmaceutical composition comprising compound 1, "wherein the ratio of bi-cyclic tautomer to monocyclic tautomer is substantially 100:0".

5.3.1 *Priority of claim 7 (Article 87 EPC)*

In order to decide whether the subject-matter of claim 7, as outlined in the preceding paragraph, enjoys the claimed priority date, it will be necessary to analyse the contents of document (6).

The composition according to claim 1 of document (6) comprises "a bicyclo-nonane compound" and "**a medium chain fatty acid triglyceride**" (emphasis added). The presence of the latter component as a mandatory feature of the compositions is repeated throughout this document (see, in particular, page 1, lines 3 to 5; page 2, line 5 to page 3, line 22; page 11, lines 6 to 9; page 13, lines 2 to 6). This feature is missing in claim 7 of the main request.

The appellant referred to the paragraph in document (6) on page 12, lines 16 to 22, as providing a basis for a general disclosure of pharmaceutical compositions without any limitation with respect to additional components. However, this paragraph relates to the manner in which "**the composition of the present invention** may be formulated" (emphasis added), and cannot therefore be read independently of the remaining description.

It is therefore concluded that the disclosure of the priority document (6) is limited to compositions containing "a medium chain fatty acid triglyceride". This is to be contrasted with the present application as originally filed, which includes claims generally directed to "a pharmaceutical composition comprising a bi-cyclic compound" (claims 4 to 6).

In addition, there is no disclosure in document (6) that could provide a basis for the tautomeric ratio of "substantially 100:0". In particular, the sentence of the application as originally filed that was cited by the appellant as providing a basis for this feature (page 12, lines 2 to 6; cf. above point VIII, third paragraph) is missing in the corresponding passage of document (6) (page 9, line 19 to page 10, line 2).

For these reasons, the board concludes that the subject-matter of claim 7 of the main request is not entitled to the priority date of 15 October 1999, but only to the filing date of 13 October 2000.

5.3.2 Document (8) was filed as an international application under the PCT on 4 September 2001, that is, after the filing date of the patent in suit. However, the document from which it claims priority, namely, document (9), was filed 5 September 2000, which is earlier than the effective date of present claim 7 (see preceding point 5.3.1). Document (8) has been published in an official language of the EPO, and the national fees have been paid for all the contracting states designated in the present application (Article 158(2) EPC 1973).

Insofar as its content corresponds to that of its priority document (9), document (8) therefore

constitutes prior art under Article 54(3) EPC and Article 54(4) EPC 1973, which are the articles applicable in accordance with the transitional provisions of the EPC 2000 (see OJ EPO 2007, special edition no. 1, 197, Article 1, paragraph 1).

Both documents (8) and (9) disclose **pharmaceutical compositions** comprising bi-cyclic halogenated compounds (see e.g. document (8), page 8, lines 7 to 9; document (9), page 4, lines 26 to 28).

Compound 1 is disclosed in document (8), on page 15, lines 1 to 6, and in document (9), on page 9, line 24 to page 10, line 4, as bicyclic "Tautomer II" having two fluorine atoms at the C-16 position (see also document (8), page 34, line 5; document (9), page 19, line 11).

In the following paragraphs (see, in particular, document (8), page 16, lines 1 to 4; and document (9), page 10, lines 12 to 15), compositions are disclosed "in which the bi-cyclic form is present in ratio of bi-cyclic/mono-cyclic of least 1:1, and preferably 20:1, or even greater to **substantially all bi-cyclic compound**". It is noted in this context that the terms "substantially all" and "substantially 100:0" were regarded by the appellant as being equivalent in meaning (cf. above point VIII, third paragraph).

In view of the above, it is concluded that document (8) and and its priority document (9) both disclose the subject-matter claimed in claim 7 of the main request.

The board is not convinced by the appellant's line of argumentation advanced in this context, based on a lack of enablement of document (8). It must be emphasised

that the relevant disclosure of the patent in suit is very similar in nature to that of documents (8) and (9) (cf., in particular, patent in suit, paragraphs [0039] and [0085] with document (8), page 15, line 7 to page 16, line 5 and table on page 38; document (9), page 10, lines 5 to 16 and table on page 22). In other words, the same level of detail is provided in all these documents with respect to the provision of the compounds and compositions disclosed. Therefore, if the appellant's argument were to be accepted with respect to document (8), the same standard would have to be applied in assessing sufficiency of disclosure of the subject-matter claimed in the main request.

Consequently, claim 7 lacks novelty within the meaning of Articles 52(1) and 54(3) EPC, and Article 54(4) EPC 1973, in view of the disclosure of document (8), which enjoys an earlier effective date than the patent in suit for the subject-matter claimed.

5.4 The main request must therefore fail for lack of novelty of claims 3 and 7 (Articles 52(1), 54 EPC).

6. Auxiliary requests 1 to 3, novelty

Claim 3 of the main request is present as claim 1 in auxiliary request 2, and claim 7 of the main request as claims 3 and 1 in auxiliary requests 1 and 3, respectively (cf. above points V to VII). Therefore, the considerations concerning novelty set out above in point 5 with respect to the main request apply equally to the auxiliary requests 1 to 3.

Consequently, auxiliary requests 1 to 3 also do not meet the requirements of novelty (Articles 52(1), 54 EPC).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated