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Datasheet for the decision of 14 November 2011

Case Number: T 1827/07 - 3.3.01

Application Number: 01967621.2

Publication Number: 1322641

IPC: C07D 09/12, A61K 31/4535, A61P 9/10, A61P 19/02, A61P 25/00, A61P 35/00

Language of the proceedings: EN

Title of invention:
Pharmaceutically active hydrophilic sulfonamide derivatives as inhibitors of protein jun-kinases

Applicant:
Merck Serono SA

Opponent:
-

Headword:
Hydrophilic sulfonamides/MERCK SERONO

Relevant legal provisions:
-

Relevant legal provisions (EPC 1973):
-

Keyword:
"Inventive step (yes) - nonobvious modification in chemical structure of the compounds of the prior art"
"Swiss-type claim"

Decisions cited:
G 0002/08

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1827/07 - 3.3.01

D E C I S I O N
of the Technical Board of Appeal 3.3.01
of 14 November 2011

Appellant: (Applicant)
Merck Serono SA
Centre Industriel
CH-1267 Coinsins, Vaud (CH)

Representative:
De Luca, Giampiero
Merck Serono SA - Geneva
Intellectual Property
9, chemin des Mines
CH-1202 Geneva (CH)

Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 15 June 2007 refusing European patent application No. 01967621.2 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman: P. Ranguis
Members: C. M. Radke
L. C. Bühler

Summary of Facts and Submissions

I. The present application relates to certain hydrophilic sulfonamide derivatives which are deemed to be useful in the treatment or prevention of disorders of the immune and neuronal systems.

II. The applicant appealed against the decision of the examining division to refuse European patent application No. 01 967 621.2.

III. The following documents were cited during examination proceedings:

(D1) WO-A-99/65 451
(D2) WO-A-00/02 851
(D3) EP-A-0 138 720.

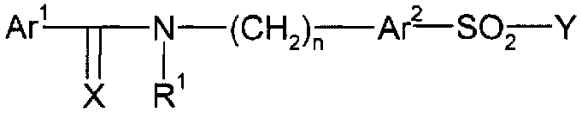
IV. The examining division decided that the subject-matter of the claims then on file was not based on an inventive step in view of the disclosure of document (D3), taking into account that it was not credible that the unlimited number of compounds claimed possessed the beneficial properties against CNS disorders.

V. The claims now on file are

- claims 1 to 5 and 7 to 9, filed under cover of the letter dated 20 June 2011, and
- claim 6, filed with the letter dated 22 September 2011.

(a) Claim 1 reads as follows:

"1. Hydrophilic sulfonamide derivatives according to formula I



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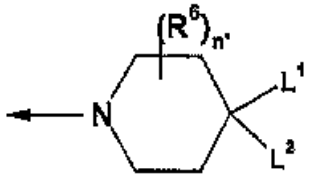
with its geometrical isomers, in an optically active form as enantiomers, diastereomers, as well as in the form of racemates and the pharmaceutically acceptable salts thereof, wherein
Ar^l is a phenyl optionally substituted by -OR wherein R is C_1-C_6 alkyl;
Ar^2 is a thienyl group carrying at least one hydrophilic substituent wherein the hydrophilic substituent is $-COOR^3$, $-CONR^3R^{3'}$, OH, C_1-C_4 alkyl substituted with OH or an amino group, a hydrazido carbonyl group, a sulfate, a sulfonate, an amine or an ammonium salt;
X is 0 or S;
R^1 is hydrogen or a C_l-C_6-alkyl group;
n is an integer from 1 to 3;
Y has the general formula



whereby, L^l and L^2 are independently selected from the group consisting of H, $-NR^{3'}R^3$, $-NR^{3'}C(O)R^3$, $-NR^{3'}C(O)NR^{3'}R^3$, $-(SO)R^3$,
$-(SO_2)R^3$, $-NSO_2R^3$, $-SO_2NR^{3'}R^3$,
with R^3, $R^{3'}$ being substituents independently selected from the group consisting of H,

C_1-C_6-alkyl, C_4-C_{18}-alkyl, C_2-C_6-alkenyl, aryl being phenyl, aryl-C_l-C_6-alkyl, being phenyl-C_l-C_6-alkyl, said aryl group being optionally substituted by halogen, hydroxy, nitro, sulfonyl;
R^6 is selected from the group consisting of hydrogen, C_l-C_6-alkyl, C_l-C_6-alkoxy, OH, halogen, nitro, cyano, sulfonyl, oxo (=O), and
n' is an integer from 0 to 4."

(b) Dependent claims 2 and 3 relate to preferred embodiments of claim 1, claim 4 to specific compounds covered by claim 1, claim 5 to the compounds claimed in the preceding claims for use as a medicament, claim 6 to their use for the preparation of a medicament against certain diseases, claim 7 to pharmaceutical compositions containing these compounds, and claims 8 and 9 to processes for making the compounds.

VI. The appellant provided the following amended pages of the description:

pages 8 to 10 and 12 to 22
under cover of the letter dated 21 September 2011; and
page 11 under cover of the letter dated 22 September 2011.

VII. The appellant referred to the decision under appeal in which the examining division acknowledged novelty of the subject-matter claimed, and to the communication of the examining division indicating that the problem of providing further sulfonamide derivatives useful in the treatment of nervous system disorders was solved. It argued that the present claims were now restricted in scope to represent a reasonable generalisation.

VIII. The appellant requested that a patent be granted on the application thus amended, or, if the board still had objections concerning the patentability, that oral proceedings be held.

Reasons for the Decision

1. The appeal is admissible.

2. For the reasons given below, the board has no objections concerning the patentability of the subject-matter claimed. Therefore, the precondition under which the appellant requested oral proceedings is not fulfilled (see point VIII above). Hence, the board could decide on the case without holding oral proceedings.

3. Article 123(2) EPC

3.1 Claim 1 is based on original claim 1,

- claims 4 and 5 (as far as the definition of Ar^2 is concerned),
- page 12, line 22 (**n** is an integer from 1 to 3),
- page 12, line 17 (**Ar^1** is a substituted or

unsubstituted aryl); page 13, line 24 (the substituent of the aryl group Ar^1 may be C_1-C_6-alkoxy); and page 8, lines 22-24 (the aryl radical may be phenyl; see also the examples, where Ar^1 always is 3-methoxyphenyl);

- page 13, lines 3-12 (as far as the definition of $\mathbf{L^1}$ and $\mathbf{L^2}$ is concerned);
- as to the substituents of the aryl groups in R^3 and $R^{3'}$: page 13, lines 13-17 and 22-27and page 8, lines 22-24 (the aryl radical may be phenyl; see also the examples 1 and 5-9 where R^3 is 3-trifluoromethylphenyl).

3.2 Claim 2 is based on original claim 6 and page 14, lines 20-27 of the description as originally filed. Claim 3 is based on original claim 7 and page 8, lines 22-24, as well as page 13, lines 1-6 of the application as originally filed. Claims 4 to 9 are based on original claims 8 to 10, 14, 15 and 20, respectively.

3.3 The amended pages of the decription merely adapt it to the amended claims.

3.4 Hence, the application as thus amended meets the requirements of Article 123(2) EPC.

4. Novelty

The examining division acknowledged that the subject-matter of the claims then on file was novel (see point 2 of the grounds for the decision under appeal). The Board has verified that this also holds for the present claims. Their subject-matter differs from the

content of any of the documents (D1) to (D3) which do not disclose compounds of the formula (I) of present claim 1 where the n is an integer of from 1 to 3. For this reason, the subject-matter of claim 1 is novel. The same holds for claims 2-9, which are limited by the same differing feature (see point V(b) above).

5. Inventive step

5.1 The closest prior art

The closest prior art is normally a document disclosing subject-matter with the same objectives as the claimed invention and having the most relevant technical features in common.

5.1.1 The application is directed to pharmaceutical compounds for the treatment or prevention of disorders of the immune and neuronal systems, specifically displaying a substantial modulatory, notably an inhibitory activity on the JNK (Jun-Kinase) function or pathways (see page 1, lines 5-13). Inhibition of Jun-Kinase may block apoptosis (programmed cell death; see page 1, lines 15-16; page 2, lines 8-10; page 4, lines 6-10). Examples of diseases to be treated are auto-immune and inflammatory ones (see page 5, line 16), Alzheimer's, Parkinson's and Huntington's diseases, epilepsy, cardiovascular disease and cancer (see page 6).

5.1.2 When determining which document could be considered as the closest prior art, it has to be borne in mind that the primary aim of the application was to provide pharmaceutical compounds useful for the treatment or prevention of certain disorders, and that the pathway

or mechanism by which these pharmaceuticals achieve the desired effect is of only secondary interest.

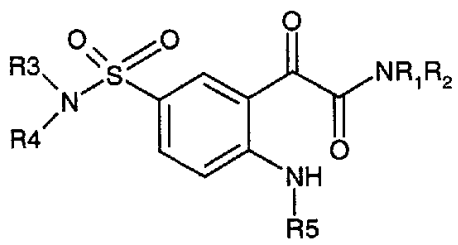
5.1.3 Document (D1) deals with the inhibition of Caspases for use in the treatment of apoptosis (see page 5, lines 24-26). The compounds could be effective against cancer, Alzheimer's and Parkinson's diseases (see page 3, lines 21, to page 5, line 13, and the table on pages 18-19).

Document (D2) relates to pharmaceutically active compounds for the therapy and prophylaxis of cardiovascular diseases, i.e. compounds capable of modulating the body's production of cyclic guanosine monophosphate (cGMP) (see page 1, lines 10-16).

Document (D3) relates to compounds having an activity on the central nervous system, especially to those having an anxiolytic activity (see page 1, lines 8-14).

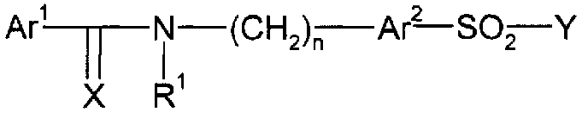
Hence, document (D1) (rather than (D2) or (D3)) relates to compounds effective against the diseases to be prevented or treated by the compounds claimed in the present application. Consequently, document (D1) is considered to represent the closest prior art.

5.1.4 The compounds claimed in document (D1) are those of the formula



(I).

When comparing these with the ones of present claim 1



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(where n= 1-3)

one notes that

- in document (D1) the sulfonyl group (i.e. the group of the formula $-SO_2-$) is directly linked to a **benzene** ring which is **directly linked** to the amino group $-NH-R^5$
- whereas present claim 1 requires the corresponding radical Ar^2 to be a substituted **thienyl** group which is linked to the $N-R^1$ group **via** the alkylene group of the formula **$-(CH_2)_n-$**.

5.2 One of the problems addressed in the application as filed was "to provide chemical compounds which are able to modulate, preferably to down-regulate or to inhibit the JNK (Jun kinase) pathway so to be useful in a method of treating diseases which involve the JNK pathway" (see page 8, lines 1-3), such as auto-immune and inflammatory ones and cancer. The table on page 37 of the application as filed shows that the compounds of examples 1, 4 and 6 do indeed inhibit the JNK3 receptor.

Taking into account the now limited scope of the claims, it is plausible that essentially all the compounds claimed show this effect and are thus suitable for the treatment of diseases involving the JNK pathway, such as auto-immune and inflammatory diseases and cancer.

The problem solved in view of document (D1) may thus be considered as providing further pharmaceutically active

compounds useful for the treatment of auto-immune and inflammatory diseases and cancer.

5.3 Document (D1) as such cannot render the subject-matter of present claim 1 obvious, as the general formula in claim 1 of document (D1) excludes the possibility that Ar^2 may be a substituted thienyl radical, let alone that it could be linked to the N-R1 group via the group of the formula $-(CH2)_n-$ (see under point 5.1.4 above).

5.4 Documents (D2) and (D3) deal with the treatment of diseases quite different from those addressed in document (D1) (see under point 5.1.3 above). Therefore, it is unlikely that the person skilled in the art would have consulted the teaching of document (D2) and/or (D3) when looking for alternative compounds to be effective against the disorders addressed in document (D1).

Furthermore, not only document (D1) but also documents (D2) and (D3) exclude the presence of an alkylene group which links the group Ar^2 with the nitrogen atom of the amino group (see (D2), the formula in claim 1, where the arylene group A^1 is directly linked to the -NH-group; see (D3), the formula in claim 1 which excludes the possibility that an alkylene group is directly linked to the benzene ring).

Hence, there is no indication in the prior art which could lead the person skilled in the art to modify the compounds disclosed in document (D1) to yield the compounds claimed in present claims 1 to 5 when trying to solve the problem posed. For this reason, the subject-matter of these claims is not deemed to be obvious. The same holds for claim 6 directed to the use

of these compounds for the preparation of a medicament against certain diseases, claim 7 directed to pharmaceutical compositions containing these compounds, and claims 8 und 9 relating to processes for making them.

Therefore, the subject-matter of the present claims is based on an inventive step.

6. Swiss-type claim 6

Claim 6 is directed to the "Use of a sulfonamide derivative according to any of claims 1-4 for the preparation of a medicament for the treatment of a neuronal disorder selected from ...". Thus it is in the form of a "Swiss-type claim".

The Enlarged Board of Appeal has decided that a claim of this type may no longer be used "Where the subject-matter of a claim is rendered novel only by a new therapeutic use ..." (see G 02/08, OJ EPO 10/2010, 456, point 7 of the reasons and the answer to question 3).

This decision applies only to patent applications having a filing date or earliest priority date of 29 January 2011 or later (see G 02/08, point 7.1.4 of the reasons, in combination with the "Notice from the European Patent Office dated 20 September 2010 concerning the non-acceptance of Swiss-type claims...", OJ EPO 10/2010, 514, point 4).

The present application is not affected by this ruling in G 02/08, as it has a priority date of 27 September 2000.

Hence, Swiss-type claim 6 may remain in the present set of claims.

7. The Board is not aware of any other deficiencies which could prejudice the grant of a patent on the present application.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent on the basis of the following documents:

   Claims:
   Nos. 1 to 5 and 7 to 9, filed with the letter of 20 June 2011; and
   No. 6, filed with the letter of 22 September 2011.

   Description:
   pages 1 to 7 and 30 to 48 as originally filed;
   pages 8 to 10 and 12 to 22 filed with the letter of 21 September 2011; and
   page 11 filed with the letter of 22 September 2011.

The Registrar: The Chairman:

M. Schalow P. Ranguis