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**D E C I S I O N**  
of 28 June 2000

**Case Number:** T 0469/97 - 3.3.1

**Application Number:** 92924151.1

**Publication Number:** 0612318

**IPC:** C07D 261/20

**Language of the proceedings:** EN

**Title of invention:**

Heteroaryl piperidines, Pyrrolidines and Piperazines and their use as Antipsychotics and Analgetics

**Applicant:**

Aventis Pharmaceuticals Inc.

**Opponent:**

-

**Headword:**

Heteroaryl piperidines, pyrrolidines and piperazines/AVENTIS PHARMACEUTICALS INC

**Relevant legal provisions:**

EPC Art. 123(2), 54(2), 111(1)  
EPC R. 88

**Keyword:**

"Main request - support in the application as filed (no)"  
"First auxiliary request - correction of obvious mistake (no) - support in the application as filed (no)"  
"Second auxiliary request - support in the application as filed (yes) - novelty (yes)"  
"Remittal to first instance for further prosecution"

**Decisions cited:**

G 0003/89; G 0011/91; T 0493/90; T 0532/95

**Catchword:**

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Boards of Appeal

Chambres de recours

Case Number: T 0469/97 - 3.3.1

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.1  
of 28 June 2000

**Appellant:** Aventis Pharmaceuticals Inc.  
10236 Marion Park Drive  
Kansas City  
Missouri 64137-1405 (US)

**Representative:** Gutmann, Ernest  
Ernest Gutmann - Yves Plasseraud S.A.  
3, rue Chauveau-Lagarde  
FR-75008 Paris (FR)

**Decision under appeal:** Decision of the Examining Division of the  
European Patent Office posted 19 November 1996  
refusing European patent application  
No. 92 924 151.1 pursuant to Article 97(1) EPC.

**Composition of the Board:**

**Chairman:** A. J. Nuss  
**Members:** P. F. Ranguis  
S. C. Perryman

## Summary of Facts and Submissions

- I. The Appellant (Applicant) lodged an appeal on 7 January 1997 against the decision of the Examining Division posted on 19 November 1996 refusing European patent application 92 924 151.1 (European publication No. 0 612 318).
- II. The decision of the Examining Division was based on claims 1 to 221 filed with letter dated 21 May 1996 in response to the first official communication. The Examining Division held that:
- the subject-matter of claims 1, 152, 169, 174, 183, 185 to 187, 191 to 200, 205 and 216 to 221 failed to satisfy the requirements of Article 123(2) EPC. The Examining Division noted, in particular, that the second disclaimer of claim 152 had been amended in such a way that different compounds were now excluded,
  - the subject-matter of claims 1, 169 and 191 failed to satisfy the requirements of Article 84 EPC and
  - the subject-matter of claims 1, 2, 10 to 64, 68, 106, 107, 152 to 154, 156, 157, 159, 162, 169 to 178 and 179 to 182 failed to satisfy the requirements of Article 54 EPC in view of the following documents:
    - (1) EP-A-0 402 644
    - (2) EP-A-0 398 425
    - (3) GB-A-2 163 432
    - (4) EP-A-0 196 096.

III. With the Statement of Grounds of Appeal, the Appellant submitted in essence that the Examining Division had not invited the Applicant as often as necessary to file his observations as provided by Article 96(2) EPC and that the refusal of the application was based on grounds or evidence on which Applicant had not had a full opportunity to present its comments contrary to the provisions of Article 113(1) EPC and requested:

- As the main request, that the contested decision be set aside for "substantial procedural violation" (Article 96(2) and Article 113(1) EPC) and the case be remitted to the Examining Division,
- As the first auxiliary request, that the European patent application be remitted to the first instance with the order to grant a patent on the basis of the refused claims 1 to 221,
- As the second auxiliary request that the European patent application be remitted to the first instance with the order to grant a patent on the basis of the claims 1 to 149 filed with the statement of grounds of appeal,
- As the third auxiliary request, that the European application be remitted to the first instance with the order to grant a patent on the basis of the claims 1 to 26 filed with the statement of the grounds of appeal.

IV. With a letter of 30 July 1999, the Appellant requested as the fourth auxiliary request that the European application be granted on the basis of another set of claims 1 to 28. With letter of 30 December 1999, the

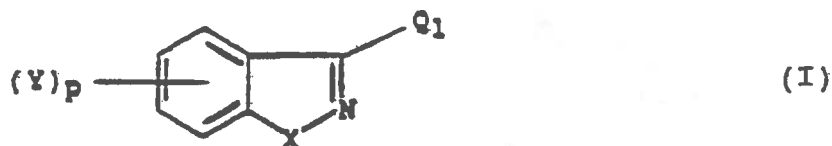
Appellant abandoned all the previous requests except the fourth auxiliary request, the latter becoming therefore the main request.

V. In response to a communication of the Board dated 2 February 2000, the Appellant submitted on 30 May 2000 as sole request a new set of claims 1 to 25 and requested that the case be remitted to the first instance for further prosecution.

VI. At the oral proceedings which took place on 28 June 2000, the Appellant submitted, in addition to the main request (see point V above), two sets of claims as auxiliary requests I (claims 1 to 28), II (claims 1 to 48), respectively. Independent claims of each request are quoted below as far as necessary in the context of this decision.

(a) Main request

1. A compound of the formula:

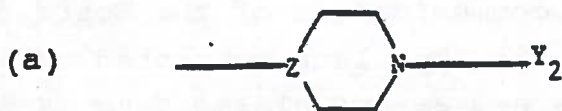


wherein

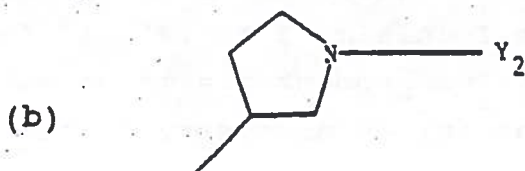
X is -O-, -S-, -NH-, or -N-R<sub>2</sub>  
R<sub>2</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, aryl C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, cycloalkyl, aroyl, alkanoyl, and phenylsulfonyl groups;  
p is 1 or 2;  
Y is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy, chlorine, fluorine, bromine, iodine, C<sub>1</sub>-C<sub>6</sub> alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is C<sub>1</sub>-C<sub>6</sub> alkoxy, hydroxy or halogen when p is 2  
and X is -O-;

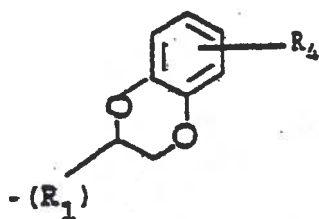
Q<sub>1</sub> is selected from the group consisting of:



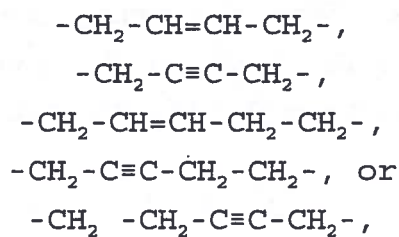
and



where Z is -CH- or -N-; and  
Y<sub>2</sub> is



in which (R<sub>1</sub>) is R<sub>20</sub>, R<sub>21</sub> or R<sub>22</sub>, wherein:  
R<sub>20</sub> is -(CH<sub>2</sub>)<sub>n</sub>- where n is 2, 3, 4 or 5;  
R<sub>21</sub> is



the -CH=CH- bond being cis or trans;

R<sub>22</sub> is R<sub>20</sub> or R<sub>21</sub> in which one or more carbon atoms of R<sub>20</sub> or R<sub>21</sub> are substituted by at least one C<sub>1</sub>-C<sub>6</sub> linear alkyl group, phenyl group or



where Z<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl, -OH, C<sub>1</sub>-C<sub>6</sub> alkoxy, -CF<sub>3</sub>, -NO<sub>2</sub>, NH<sub>2</sub> or halogen;

R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, hydroxy, amino, mono- or dialkylamino, C<sub>1</sub>-C<sub>3</sub> acyl amino, C<sub>1</sub>-C<sub>6</sub> alkanoyl, trifluoromethyl, chlorine, fluorine, bromine, -O-C(=O)-(C<sub>1</sub>-C<sub>12</sub> straight or branched chain) alkyl or -C(=O)-aryl; in which aryl is phenyl or



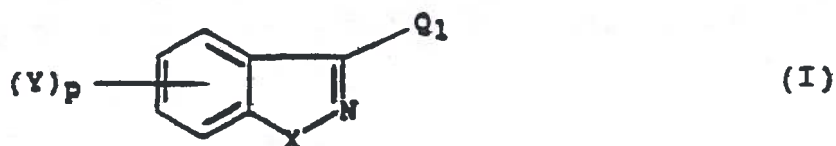
where R<sub>5</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, C<sub>1</sub>-C<sub>6</sub> monoalkylamino, C<sub>1</sub>-C<sub>6</sub> dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

with the proviso that in formula (I), Z is not

$\begin{array}{c} | \\ -N- \end{array}$ , when X is -S-, Y is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy, halogen, C<sub>1</sub>-C<sub>6</sub> alkoxy, CF<sub>3</sub>, R<sub>1</sub> is -R<sub>20</sub>-, and R<sub>4</sub> is hydrogen;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid addition salt thereof.

23. 6-aceto-2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]-methyl-1,4-benzodioxan; or 2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]-methyl-1,4-benzodioxan, or a pharmaceutical acceptable acid addition salt thereof.
24. A pharmaceutical composition comprising a compound according to any one of claims 1 to 23 and a pharmaceutically acceptable carrier.
25. Use of a compound having one of the formula I or I' for the preparation of a medicament for treating psychoses, where I is as defined in claim 1 and I' represents

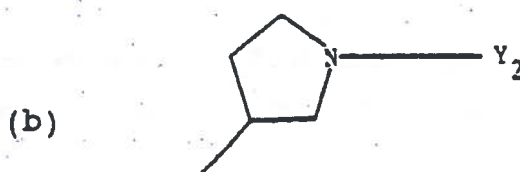


wherein

X, R<sub>2</sub>, p, Y, are as defined in claim 1,  
Q<sub>1</sub> is selected from the group consisting of:

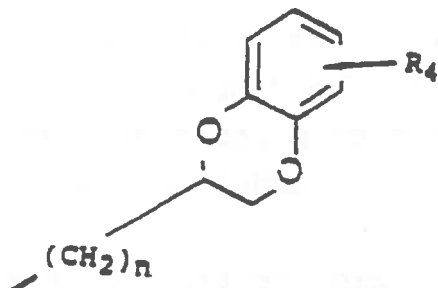


and





where Z is  $\overset{|}{-CH-}$  or  $\overset{|}{-N-}$ ; and  
Y<sub>2</sub> is



in which:

n is 1 or 2;

$R_4$  is hydrogen or  $-C(=O)-CH_3$

all geometric, optical and stereoisomers thereof,  
or a pharmaceutically acceptable acid addition  
salt thereof.

(b) **First auxiliary request**

The first auxiliary request differs essentially  
from the main one in that the proviso of claim 1  
was amended to read:

"with the proviso that in formula (4)  $R_4$  is not H  
when  $R_1$

is  $R_{20}$ , Z is  $\overset{|}{-N-}$  (emphasized by the Board), X is -  
S-, Y is hydrogen, halogen, lower alkyl, lower  
alkoxy, hydroxy or trifluoromethyl, and p is 1 or  
2;"

A new product claim 19 was added related  
essentially to the compound of formula I' as  
defined in the claim 25 of the main request.

(c) **Second auxiliary request**

The second auxiliary request differs essentially from the main one in that:

- in claim 1, the substituent Z is <sup>1</sup>-N- was cancelled (the compounds of formula (I) being restricted to piperidine derivatives) and the proviso was amended to read  
  
"with the proviso that R<sub>4</sub> is not H when R<sub>1</sub> is R<sub>20</sub>, Z is not <sup>1</sup>-N-, X is -S-, Y is hydrogen, halogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, hydroxy or trifluoromethyl, and p is 1 or 2;"
- in use claim 23 (which corresponds essentially to the claim 25 of the main request), the proviso was deleted and the formula (b) of the substituent Q<sub>1</sub> in formula I' was cancelled.
- dependent use claims 24 to 48 are based on the dependent product claims 2 to 22.

VII. The Appellant's submissions both in the written proceedings and at the oral proceedings can be summarised as follows:

VII.1 Although the proviso present in claim 1 of the main request excluded piperazine compounds, while the proviso as filed excluded the corresponding piperidine compounds, this change was supported by document (3) which disclosed the excluded piperazine compounds.

VII.2 In the wording of the proviso of claim 1 of the first auxiliary request, the deletion of the word "not" was to be considered as the correction of an obvious mistake which should be allowed according to Rule 88

EPC. In particular, it was clear, in view of the description as filed that among the seventeen provisos present, only the proviso at stake contained a double negation and, therefore, the man skilled in the art would have noted that an error was present. Moreover, most of the examples related to piperidine compounds and the proviso of the application as filed was not in line with the said disclosure taken as a whole. The correction was furthermore obvious in view of the disclosure of document (3).

VII.3 The subject-matter of the claims of the three requests (main request, first and second auxiliary requests) directed to the compounds or to pharmaceutical compositions was novel over document (3). Concerning the subject-matter of the claims directed to the use of compounds for treating psychoses, the disclosure of document (3) showed no evidence of any tests effectively carried out to determine the antipsychotic effect of the disclosed compounds. It was, in particular pointed out that the tests described page 6, lines 5 to 37 related to the measure of the drugs's analgesic activity.

VIII. The Appellant requested that the decision be set aside and that the matter be remitted to the first instance for further prosecution on the basis of the claims of the main request of 26 May 2000, or of the claims of the first or second auxiliary request submitted at the oral proceedings on 28 June 2000.

IX. At the end of the oral proceedings the decision of the board was given orally.

## Reasons for the Decision

1. The appeal is admissible.

### *Main request*

2. *Article 123(2) EPC - Fair basis*

- 2.1 The Appellant admitted in the course of the oral proceedings that claim 1 of the main request contained a proviso excluding piperazine compounds, while a proviso excluding piperidine compounds was present in the description and claims as filed. This amounts to the incorporation of a material (piperidine compounds) originally excluded. The present claim 1 extends, therefore, beyond the content of the application as filed and does not meet the requirement of Article 123(2) EPC.

- 2.2 For this reason the present main request is not allowable.

### *First auxiliary request*

3. *Article 123(2) - Rule 88 EPC Corrections of errors*

- 3.1 The Appellant submitted that an error had occurred in the description of the application as filed so that its text did not conform to what was intended and he sought to correct that error in order to bring the text and the claim 1 of the present request into conformity with the intended wording.

3.2 In order for a correction under Rule 88, second sentence, EPC to be allowable, it must be established

- (a) that an error is in fact present in the document filed at the EPO, and
- (b) that the correction of the error is obvious in the sense that it is immediately evident that nothing else would have been intended than what is offered as the correction.

(see T 493/90 of 10 December 1991, point 2 and T 532/95 of 4 March 1999, point 3.2.1 of the reasons for the decision).

3.3 With respect to the above requirement (a), the application in suit as filed must contain such an **obvious** error that a skilled person has no doubt that this information is not correct and - considered objectively - cannot be to read as such (see opinion G 3/89 and decision G 11/91, OJ EPO 1993, 117 and 125, point 5 of the reasons for the decision). In the present case the proviso present in the description as filed excludes some piperidine compounds as admitted by the Appellant. The Board notes, first, that this proviso is clear in the sense there is no ambiguity as to the excluded compounds. The argument of the Applicant regarding the non compliance of the said proviso with the examples is not convincing given that the Appellant has not shown that any example fell within the definition of the proviso. There is no discrepancy between the examples and the said proviso. Furthermore, the double negation present in the said proviso is certainly not in line with the wordings of the other provisos. However, as already mentioned, this singular wording does not lead to any ambiguity and given that it is the sole expression used in the

application as filed (page 15, bottom paragraph; page 28, third paragraph; claim 1, page 210, third paragraph; claim 191, page 268, third paragraph; claim 192, page 277, third paragraph and claim 194, page 295, third paragraph), it cannot be deduced therefrom that an error is present. The other argument regarding the fact that this proviso was intended to exclude the compounds of document (3) is also not acceptable because document (3) is not cited in the application as filed, so this is not an intention the reader could deduce from the original application text.

3.4 It is the Board's conclusion that the new wording of the proviso present in claim 1 of the present request is not allowable as a correction under Rule 88 EPC and, therefore, that the subject-matter of claim 1 of the first auxiliary request extends beyond the content of the application as filed contrary to the requirement of Article 123(2) EPC.

4. *Second auxiliary request*

4.1 *Articles 123(2) and 84 EPC*

4.2 The subject-matter of claim 1 is based on the claim 1 of the application as originally filed with the further restriction to compounds of formula (I) wherein  $Y_2$  is a benzodioxan-2-yl hydrocarbylene group of formula (4) and that expressions such as "lower" alkyl or alkyleneyl mean " $C_1-C_6$ " (see page 18, lines 14 ff. of the application as filed), the substituent (a) being itself limited to the piperidine moiety (Z is -CH-).

4.3 The Board sees no objection under Article 123(2) EPC against the present claim 1. In particular, the restrictions set out in point 4.2 above do not amount to a selection of a specific sub-class of compounds not

disclosed in the application as filed but, on the contrary, consist of a limitation to possibilities each of which was already disclosed in the application as filed. The claim is also clear.

4.4 However, the Board has noted that the term "<sup>1</sup>Z is not -N-" present in the wording of the proviso was redundant as this meaning had been cancelled (see point 4.2 above). Such a correction is left to the Appellant and the Examining Division in the subsequent prosecution.

4.5 The subject-matter of dependent claims 2 to 22 is supported by the application as filed:

- claims 2 to 9 are respectively supported by the application as filed, namely claim 95; claim 153; claim 154; claim 157; claim 158; claim 159; claim 160; claim 161.
- claims 10 to 16 are supported by the application as filed page 31, first and second paragraph and page 18, lines 14 ff.
- claim 17 is supported by the application as filed, page 34, line 9.
- claims 18 to 20 are supported by the application as filed, page 64, first paragraph.
- claim 21 is supported by the application as filed, namely claims 93 and 94.
- claim 22 is supported by the application as filed, namely claim 191 (see last two lines).

Those claims are also clear within the meaning of Article 84 EPC.

4.6 The subject-matter of independent claim 23 is based:

- for the compounds of formula (I) on the claim 193 of the application as originally filed with the further restriction to the compounds of formula (I) wherein Y<sub>2</sub> is a benzodioxan-2-yl hydrocarbylene group of formula (4) and
- for the compounds of formula (I') on the description, pages 30 to 32; page 20, seventh paragraph; pages 17 to 18, bridging paragraph and page 18, lines 14 ff. The Board sees no objection under Articles 123(2) and 84 EPC for the same reasons as set out at point 4.3 above.

4.7 The subject-matter of dependent claims 24 to 48 is supported by the application as filed.

- claim 24 is supported by originally filed claim 193 and page 18, lines 14 ff.,
- claims 25 to 34 are respectively supported by the application as filed, namely claim 95; claim 153; claim 154; claim 155; claim 156; claim 157; claim 158; claim 159; claim 160; claim 161,
- claims 35 to 41 are supported by the application as filed page 31, first and second paragraph and page 18, lines 14 ff.,
- claim 42 is supported by the application as filed, page 34, line 9,
- claims 43 to 45 are supported by the application as filed, page 64, first paragraph,



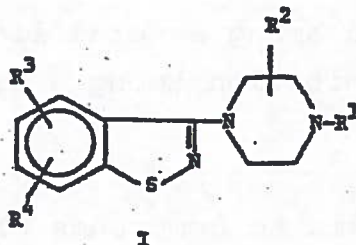
- claim 46 is supported by the application as filed, page 32. The restriction of the compounds of formula (I') to those where n is 2 does not amount to a selection among several lists but to an admissible limitation among a single list (n is 1 or 2),
- claim 47 related to compounds of formula (I') according to claim 23 is supported by the description of the application as filed for the same reasons as set out in point 4.6. However, the Board has noticed subsequently that the group (b) had been kept on while it is obvious that this group is no longer in line with the claim 23 and furthermore it was the intention of the Appellant to limit the scope of claim 23 and, as a result, of the therefrom depending claim 47. Such a correction is left to the Appellant and the Examining Division,
- claim 48 is supported by the claims 93 and 94 as originally filed.

Those claims are also clear within the meaning of Article 84 EPC.

5. *Novelty - Article 54(2) EPC*

5.1 After examination of the disclosures of documents (1), (2) and (4), the Board has reached the conclusion that the subject-matter as defined in the claims of the second auxiliary request is novel. Since, in the decision under appeal or in the course of the examination proceedings, the Examining Division acknowledged the novelty of the now claimed subject-matter with respect to those documents, it is not necessary to give detailed reasons for this finding.

- 5.2 Document (3) relates to 1,2-benzisothiazol-3-yl-piperazine derivatives having analgesic properties of formula:



wherein  $R_1$  is, in particular, a benzodioxan-2-yl-lower alkylene group (see page 2, lines 33 to 51).

- 5.3 In the Board's judgment, claims 1 to 22 directed to heteroaryl piperidine derivatives are novel in view of the disclosure of document (3). The claims 23 to 48, directed to the use of compounds for the preparation of a medicament for treating psychoses, are also novel since document (3) describes only compounds having analgesic activity.

6. *Remittal*

- 6.1 The amendments made overcome the objections pursuant to Articles 84, 123(2), 54(2) EPC which led to refusal of the application in the decision under appeal. The examination not yet having been concluded, the Board exercises its power under Article 111(1) EPC to remit the case to the Examining Division for further prosecution.
- 6.2 As mentioned in points 4.4 and 4.7, the Board has noted a redundancy in claim 1 and a discrepancy in claim 47, namely:

- in the proviso of claim 1, the term " $Z$  is not  $-N-$ " is redundant,

- in dependent claim 47 the group  $Q_1$  formula (b) should be deleted to put this claim in compliance with independent claim 23.


Moreover, in dependent claim 2 the word "salt" should be added between the last two words of that claim in order to correct an obvious omission and in claim 23 the second signification "lower" alkyl for Y in formula (I) need to be amended into " $C_1-C_6$ " for reasons of consistency.

## Order

For these reasons it is decided that:

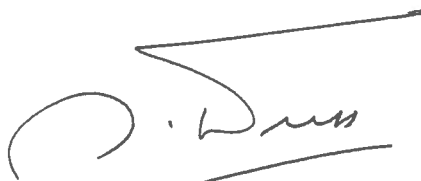
1. The decision under appeal is set aside.
2. The matter is remitted to the first instance for further prosecution on the basis of the claims of the second auxiliary request submitted at oral proceedings on 28 June 2000.

The Registrar:



N. Maslin

The Chairman:



A. Nuss

The following information was obtained from the records of the  
United States Department of Justice, Bureau of Prisons, dated  
the 15th day of August, 1954.

Records in connection with the case of the above named  
individual show that he was born on the 15th day of  
October, 1910, at Chicago, Illinois, and is now  
the inmate of the Federal Reformatory for Male Prisoners,  
Joliet, Illinois, where he is serving a term of  
one year and six months for the crime of  
kidnaping.

Very truly yours,  
Special Agent in Charge

Enclosed for the Bureau are two copies of a  
report of the Joliet Reformatory dated August 10, 1954.

Very truly yours,  
Special Agent in Charge