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**D E C I S I O N**  
**of 28 September 2005**

**Case Number:** W 0005/05 - 3.3.01

**Application Number:** PCT/US 03/28453

**Publication Number:** WO 2004/024731

**IPC:** C07D 491/04

**Language of the proceedings:** EN

**Title of invention:**

Antidepressant arylpiperazine derivatives of heterocycle-fused benzodioxans

**Patentee:**

WYETH

**Opponent:**

-

**Headword:**

Antidepressants/WYETH

**Relevant legal provisions:**

PCT Art. 34(3)(a)

EPC Art. 150(2)

PCT R. 13, 66, 68(2)(3)

**Keyword:**

"Lack of unity *a posteriori* - (no) "

**Decisions cited:**

-

**Catchword:**

-



Case Number: W 0005/05 - 3.3.01

International Application No. PCT/US 03/28453

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.01  
of 28 September 2005

**Applicant:** WYETH  
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**Decision under appeal:** Protest according to Rule 68.3(c) of the Patent Cooperation Treaty made by the applicants against the invitation of the European Patent Office (International Preliminary Examining Authority) to restrict the claims or pay additional fees dated 22 June 2004.

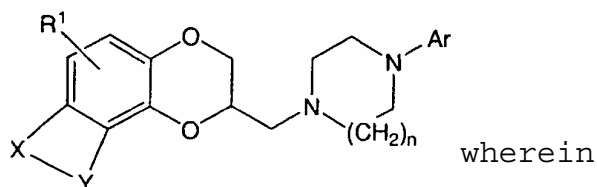
**Composition of the Board:**

**Chairman:** A. J. Nuss  
**Members:** P. P. Bracke  
M. B. Günzel

## Summary of Facts and Submissions

I. International patent application PCT/US 03/28453 was filed on 11 September 2003 with fifty six claims. Claim 1 read as follows:

"1. A compound of formula I:



R' is hydroxy, halo, cyano, carboxamido, carboalkoxy of 2 to 6 carbon atoms, trifluoromethyl, alkyl of 1 to 6 carbon atoms, alkanoyloxy of 2 to 6 carbon atoms, amino, mono- or di-alkylamino in which each alkyl group has 1 to 6 carbon atoms, alkanamido of 2 to 6 carbon atoms, or alkanesulfonamido of 1 to 6 carbon atoms;

the group X-Y is  $-N=C(R^2)-C(R^3)=N-$ ,  $-N=C(R^2)-C(R^4)=CH-$ ,  $-N=C(R^2)-N=CH-$ ,  $-N=C(R^2)-O-$ , or  $-NH-C(R^5)=CH-$ ;

R<sup>2</sup> and R<sup>3</sup> are, independently, hydrogen, halo, amino, mono- or di-alkylamino in which each alkyl group has 1 to 6 carbon atoms or alkyl of 1 to 6 carbon atoms;

R<sup>4</sup> is hydrogen or alkyl of 1 to 6 carbon atoms;

R<sup>5</sup> is hydrogen, halo, trifluoromethyl, pentafluoroethyl or alkyl of 1 to 6 carbon atoms;

Ar is phenyl, naphthyl, indolyl, indazolyl, thienyl, pyridinyl, pyrimidinyl, quinolinyl, benzofuranyl, benzothienyl, benzoisothiazolyl, or benzisoxazolyl, each optionally substituted with one to three substituents independently selected from hydroxy, halo, cyano, carboxamido, carboalkoxy of 2 to 6 carbon atoms, trifluoromethyl, alkyl of 1 to 6 carbon atoms, alkanoyloxy of 2 to 6 carbon atoms, amino, mono- or di-alkylamino in which each alkyl group has 1 to 6 carbon atoms, alkanamido of 2 to 6 carbon atoms, or alkanesulfonamido of 1 to 6 carbon atoms; and

n is 1 or 2;

or pharmaceutically acceptable salts thereof."

Claims 2 to 48 were dependent on Claim 1. The remaining claims were related to a method of treating a subject, a pharmaceutical composition, a compound for use as a medicament and the use of a compound in the preparation of a medicament for the treatment of *inter alia* depression.

- II. On 22 June 2004 the European Patent Office (EPO), acting as an International Preliminary Examining Authority (IPEA), informed the applicant that the application did not comply with the requirement of unity of invention and invited him to restrict the claims or to pay five additional examination fees pursuant to Article 34(3)(a) and Rule 68.2 PCT within a period of one month.

In an annex to this invitation the IPEA submitted that the application related to structurally distinct groups of compounds, namely:

1. Claims 1(part)-5(part), 7-8, 49(part)-56(part) directed to compounds of the formula I, where X-Y form  $-N=C(R^2)-C(R^3)=N-$ ;

2. Claims 1(part)-5(part), 6, 11-35, 37-41, 49(part)-56(part): directed to compounds containing the  $\{[2,3]$ -dihydro $[1,4]$ dioxine $[2,3-f]$ quinolin-2-yl $\}$ methyl-piperazin 1-yl-moiety, (the X-Y form  $-N=C(R^2)-C(R^4)=CH-$  (pyridine ring));

3. Claims 1(part)-5(part), 49(part)-56 (part) directed to compounds of the formula I, where X-Y form  $-N=C(R^2)-N=CH-$ ;

4. Claims 1(part)-5(part), 36, 49(part)-56(part) directed to compounds of the formula I, where X-Y form  $-N=C(R^2)-O-$ ;

5. Claims 1(part)-5(part), 9-10, 49(part)-56(part) directed to compounds of the formula I, where X-Y form  $-NH-C(R^5)=CH-$  and n is 1; and

6. Claims 1(part)-5(part), 42-48, 49(part)-56(part) directed to compounds of the formula I, where n is 2.

In particular, the IPEA found that 1,4-benzodioxan-2-yl)-methyl-piperazines were known from documents

(1) WO-A-98/16530;

(2) US-A-5 869 490; and

(3) WO-A-91/13872

as useful compounds in the treatment of drug addiction such as the addiction of ethanol or cocaine. Thus, the 1,4-benzodioxan-2-yl)-methyl-piperazine structure could no longer be seen as a special technical feature within the meaning of Rule 13 PCT. Since there was no other special feature forming a technical relationship between the inventions, the requirement of unity under Rule 13 PCT was not fulfilled.

III. By letter of 19 July 2004, the applicant paid five additional fees under protest pursuant to Rule 68.3(c) PCT and in his reasoned statement he submitted that the claimed compounds shared a novel common structural feature.

IV. On 20 October 2004, in a first written opinion pursuant to Rule 66 PCT, the IPEA repeated its non-unity objection as formulated in the invitation to pay additional fees of 22 June 2004 and discussed *inter alia* the issues of novelty and inventive step.

V. On 21 February 2005, the IPEA issued a communication informing the applicant that after a prior review of the justification for the invitation to pay additional fees, the requirement to pay the same was upheld. The applicant was thus invited under Rule 68.3(e) PCT to pay the protest fee.

VI. By letter dated 4 March 2005, the applicant paid the protest fee and requested the reimbursement of the additional examination fees and the protest fee. As reason for the reimbursement, the applicant submitted that

- (a) the compounds of Claim 1 represent a "special technical feature" for the purpose of Rule 13.2 PCT,
- (b) the IPEA failed to submit a first written opinion and to give the applicant the opportunity to reply as required according to the Guidelines under the PCT before it submitted the invitation to restrict or to pay additional fees and
- (c) the invitation to pay the protest fee was not justified because the IPEA set too short a period for response.

VII. On 24 March 2005 the IPEA sent the completed International Preliminary Examination Report (IPER) to the International Bureau of WIPO and to the applicant.

VIII. By telefax of 18 August 2005, the applicant provided a copy of a communication pursuant to Article 96(2) EPC from the EPO as elected office, dated 8 August 2005, requiring the applicant to restrict the claims due to lack of unity of the invention. The applicant submitted that the lack of unity made by the IPEA at the international stage had not yet been considered by the Board of Appeal to which the matter had been referred. Therefore, it was not clear to the applicant why he should be called upon to restrict the claims in

proceedings under the regional phase before the EPO. Moreover, the applicant was of the opinion that the IPEA had given the EPO as elected office premature access to the international preliminary examination file in contravention of obligations under Article 38(1) PCT.

- IX. Besides the reimbursement of the additional fees and the protest fee, the applicant requested that the text of both the protest and the decision thereon should be notified to the elected Offices as an annex to the international preliminary examination report as foreseen by Rule 68.3(c) PCT.

### **Reasons for the Decision**

1. The protest is admissible.
  
2. According to Rules 13.1 and 13.2 PCT the requirement of unity of invention may only be fulfilled if a group of inventions is so linked as to form a single **general inventive concept**, i.e. if there is a technical relationship among the inventions involving one or more of the same or corresponding technical features, wherein by the expression "special technical features" those technical features are meant that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.
  - 2.1 The IPEA was of the opinion that the claimed compounds and those disclosed in the cited prior art documents were known to be useful for treating the same diseases as the claimed compounds, namely the addiction to



ethanol and cocaine and depression. The finding that the claimed compounds have the combined properties of inhibiting serotonin reuptake and being antagonists of the 5HT<sub>1A</sub> receptor was only a finding of their biological mechanism, which cannot be considered a feature differentiating them from a structurally close related class of compounds.

- 2.2 Although it is true that the presently claimed compounds are taught on page 26, line 13, also to be useful for the treatment of cocaine and alcohol addiction, they are, more generally, taught both to inhibit serotonin reuptake and to be antagonists of the 5HT<sub>1A</sub> receptor and due to this combined activity to enable a more rapid onset of antidepressant efficacy (see the present application page 2, third paragraph and page 26, first paragraph).
- 2.3 Documents (1) and (2) disclose compounds having a chemical structure differing from the presently claimed ones essentially by the fact that the group X-Y represents a radical of formula -NH-CO-CO-. Such compounds are taught to have antipsychotic activity and to modulate dopaminergic neurotransmission. Thereby, they are useful in the treatment of drug addiction such as the addiction to ethanol or cocaine and related illnesses (see document (1), page 2, lines 16 and 17, and page 9, lines 5 to 13, and document (2), column 2, lines 26 and 27, and column 8, line 57 to column 9, line 2).
- 2.4 Document (3) discloses compounds differing from the presently claimed ones essentially by the presence of a piperidine ring instead of a piperazine ring. These

compounds are taught to exhibit 5HT<sub>1A</sub> binding and dopamine receptor binding activity and therefore to be useful in the therapeutic treatment of cardiovascular system and central nervous system disorders which are related to 5HT<sub>1A</sub> and/or dopamine pathways (see page 4, lines 26 to 29). Moreover, on page 6, lines 21 and 22, it is stated that the compounds may be effective as antidepressant agents.

- 2.5 However, documents (1), (2) and (3) are silent about a more rapid onset of antidepressant efficacy due to the combined activity of inhibiting serotonin reuptake and being antagonists of the 5HT<sub>1A</sub> receptor.
- 2.6 Since thus none of the cited documents discloses a compound as presently claimed nor relates to a more rapid onset of antidepressant efficacy, it is this more rapid onset, as a therapeutic effect, that defines the contribution over the prior art and represents the "special technical feature" that links the compounds of Claim 1 together in such a way that they form a single general inventive concept.
- 2.7 This finding is in agreement with the instructions concerning unity of invention, as described in the first part of annex B of the administrative instructions PCT, points (f)(i) to (iii), namely that the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2 PCT, shall be considered to be met when the claimed alternatives are of a similar nature, namely when all alternatives defined by the Markush formula have a common property or activity and that all

- alternatives belong to a recognised class of chemical compounds in the art to which the invention pertains.
- 2.8 Therefore, the Board cannot follow the IPEA's reasoning according to which the claimed subject-matter is not considered to comply with the requirement of unity of invention. Hence, the invitation provided for in Article 34(3)(a) and Rule 68.2 PCT to pay an additional fee was not justified.
3. In the light of the findings under point 2 above, there is no need to consider applicant's submissions as presented under point VI (b) and (c) above.
4. In application of Article 150(2) EPC, the board's function is limited to supplementing the express provisions of PCT Rule 68.3(c) PCT, which relate only to the examination of protests against the charging of additional fees undertaken by the IPEA. Since, thus, any activity of the EPO as elected office is not within the competence of the present board acting as special instance of the IPEA according to Rule 68.3(c) PCT, the present board does not have the competence to consider applicant's submissions presented under point VIII above.

**Order**

**For these reasons it is decided that:**

1. The additional examination fees and the protest fee paid by the Applicant are refunded.
2. The text of both the protest and this decision shall be notified to the elected Offices as an annex to the international preliminary examination report.

The Registrar:

The Chairman:

N. Maslin

A. Nuss