

Internal distribution code:

- (A) Publication in OJ
(B) To Chairmen and Members
(C) To Chairmen
(D) No distribution

**Datasheet for the decision
of 4 June 2009**

Case Number: T 0532/06 - 3.3.02

Application Number: 01103963.3

Publication Number: 1125581

IPC: A61K 3/135

Language of the proceedings: EN

Title of invention:

Use of sertraline to treat panic disorder

Applicant:

PFIZER INC.

Opponent:

-

Headword:

USE OF SERTRALINE/PFIZER INC.

Relevant legal provisions:

EPC Art. 56

Relevant legal provisions (EPC 1973):

-

Keyword:

"The request on file does not fulfill the requirements of inventive step"

Decisions cited:

-

Catchword:

-



Case Number: T 0532/06 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 4 June 2009

Appellant: PFIZER INC.
235 East 42nd Street
New York, N.Y. 10017 (US)

Representative: Ruddock, Keith Stephen
Pfizer Limited
European Patent Department
Ramsgate Road
Sandwich
Kent CT13 9NJ (GB)

Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 23 November 2005
refusing European application No. 01103963.3
pursuant to Article 97(1) EPC 1973.

Composition of the Board:

Chairman: U. Oswald
Members: M. C. Ortega Plaza
T. Karamanli

Summary of Facts and Submissions

I. European patent application EP-A-1 125 581, based on application No. 01 103 963.3, was filed as a divisional application of the parent application EP-A-0 429 189 (filed as application No 90 311 797.6). Claim 1 (single claim) read as follows:

"1. The use of the compound (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphtalenamine or a pharmaceutically acceptable salt thereof for the manufacture of a medicament to treat or prevent panic disorder and the symptoms associated with such a disorder."

II. The following documents and exhibits have been cited *inter alia* during the examination and appeal proceedings:

(1) David V. Sheehan et al, J. Clin. Psychiatry, 49(8(Suppl), 30-36, 1988

(2) C.L. Broekkamp et al, Psychopharmacology, vol 89(4), page S9, 1986

(3) Graham D. Burrows, et al, J. Clin. Psychiatry, 49(8(Suppl), 18-22, 1988

(E1) Copy of approval of the FDA (US Food and Drug Administration) dated 20 September 2002, addressed to Pfizer Pharmaceuticals

III. The appeal lies from the decision of the examining division refusing the patent application under

Article 97(1) EPC 1973 pursuant to the requirements of Article 56 EPC 1973.

IV. The examining division considered that the claim (set of claims containing one single claim) filed the 29 May 1991 (only request filed) met the requirements of novelty Article 52(1) and 54 EPC 1973.

However, the examining division was of the opinion that the subject-matter claimed lacked an inventive step (Article 56 EPC 1973).

In particular, the examining division considered document (1) to be the closest prior art. The examining division defined the problem to be solved as the provision of further agents for the treatment of panic disorders.

The examining division was of the opinion that "although the original application itself does not contain any proof to this end apart from mere statements" the problem was solved in view of the FDA approval dated 20 September 2002 submitted by the applicant at the oral proceedings before the examining division.

The examining division considered that the proposed solution, i.e. to use (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphtalenamine (sertraline) was obvious in light of document (1).

V. The appellant lodged an appeal against this decision and filed with its grounds of appeal a further document, document (3).

- VI. The board sent a communication as an annex to the summons to oral proceedings pursuant to Article 15(1) RPBA. In said communication the board conveyed a detailed preliminary opinion in relation to the issue of inventive step.
- VII. The appellant filed a letter dated 27 February 2009 announcing that it would not attend the oral proceedings. However, the appellant chose not to comment to the substance of the board's communication sent as an annex to the summons. Moreover, the appellant did not withdraw its request for oral proceedings (Article 116 EPC), which was filed with its grounds of appeal.
- VIII. Oral proceedings took place on 04 June 2009 in the absence of the appellant.
- IX. The appellant's arguments submitted with the grounds of appeal can be summarised as follows:

Panic disorder was a specific disorder categorised by symptoms of fear and panic caused by particular situations or thoughts. It was a complex disorder that still remains difficult to treat and which often required a long term treatment regime before efficacy could be established. Moreover, since there was no predictive animal model, clinical trials in patients had to be conducted to establish efficacy in treating panic disorder.

The appellant accepted document (1) as the closest prior art and defined the problem to be solved as "to

find a compound that can be used to safely and effectively treat panic disorder and the associated symptoms".

An FDA approval letter dated 20 September 2002 (E1) showed that sertraline was safe and effective in the treatment of panic disorder. This provided firm evidence that the problem was indeed solved by the claimed "invention".

It had not been obvious from the review article document (1) that sertraline would be a solution to the stated problem with an expectation of success. There was no suggestion in document (1) that sertraline would be efficacious in treating panic disorder. Document (1) was an early review article exploring the potential of serotonin reuptake inhibitors (SRIs) in treating panic disorder. However, the analysis made in document (1) was made on the basis of preliminary results and the underlying mechanism causing panic disorder was acknowledged as being unclear. Studies on only one SRI were reported, zimetidine. This compound, although shown to have efficacy in treating panic disorder was withdrawn quickly for serious safety reasons. This would discourage the skilled person from using other SRI in treating panic disorder. Document (1) had to be regarded at best to relate to a speculative teaching that a selective serotonin reuptake inhibitor (SSRI) such as sertraline was effective and safe for treating panic disorder.

Hence, at the priority date of the application in suit sertraline was only known to have antidepressant activity. Accordingly, at the priority date "it would

not have been obvious to try sertraline with an expectation of success in finding it to be a safe and efficacious drug for treating panic disorder". Thus, the claimed "invention" involved an inventive step.

Document (2) added little merit to the teaching of document (1) since even if marble burying by mice was investigated as a predictive model for nervousness and anxiety treatment, it did not relate to the study of panic disorder specifically. The marble model lacked validity as a predictive model of panic disorder in humans.

No comments were filed by the appellant to the board's communication sent as an annex to the summons to oral proceedings.

- X. The appellant had requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of claim 1 according to the sole request filed on 19 February 2001.

Reasons for the Decision

1. *Admissibility*

- 1.1 The appeal is admissible.

2. *Procedural matters*

The duly summoned appellant did not attend oral proceedings, as announced with its letter of 27 February 2009. The board was in a position to decide

at the conclusion of the oral proceedings, since the case was ready for decision (Article 15(5) and (6) RPBA) and the voluntary absence of the appellant was not a reason for delaying a decision (Article 15(3) RPBA).

3. Main request (sole request)

3.1 *Inventive step*

3.1.1 Claim 1 (single claim) which is drafted as a second (or further) medical use claim in "Swiss-type" form, relates to the use of sertraline to treat or prevent panic disorder and the symptoms associated with such a disorder.

It is a general principle that if a patent application **discloses** a (new and inventive) technical effect of a known compound, use claims may be granted based thereupon.

Although it is not a prerequisite for the granting of an application to include actual technical data (animal models or clinical data), it is a *condition sine qua non* that it is shown that the technical problem underlying the application was at least plausibly solved at the priority date. Neither the present application nor the parent application contain any technical evidence or data in relation to any of the uses of sertraline mentioned in the parent application (in particular, there is no technical evidence in the application as filed in relation to the treatment or prevention of panic disorder by using sertraline).

- 3.1.2 The board agrees with the examining division and the appellant in the choice of document (1) as closest prior art.
- 3.1.3 The appellant has defined the problem to be solved as "to find a compound that can be used to **safely and effectively** treat panic disorder and the associated symptoms" and has pointed to the FDA approval letter of 20 September 2002 for showing that the problem has been actually solved.

It has to be kept in mind that the filing date of the present application is 29 October 1990, and that the present application claims a priority of 2 November 1989. The submissions to FDA (mentioned in said FDA letter) were dated 29 April 2002.

Therefore, the long time elapsed between the effective filing date of the application and the actual data mentioned in the FDA letter does not allow to conclude that they are a valid support for the disclosure of the technical effect at the effective date of the present application.

Moreover, the application as filed does not explicitly mention that sertraline may be used **safely and effectively** to treat panic disorder. Therefore, the only disclosure of a technical effect in the application as filed is of a general nature. Hence, the content of the present application has to undergo the same plausibility check as that to be performed for the content of document (1) in relation to the disclosure of selective serotonin reuptake inhibitors in the treatment of panic disorder.

In other words, the problem of the "**actual** provision" of a method for effectively and safely treating or preventing panic disorder has not been solved by the present application, since the application does not contain any verification (or indication of such a verification) regarding sertraline as actually effective against panic disorder.

In fact, the present application merely contains a statement which has the same level of credibility as that of the statements in document (1) and amounts to analogous expectations of success for sertraline as those expressed in the prior-art document.

Thus, it can in principle be assumed that at the effective date of the present application the use of sertraline for the prevention and treatment of panic disorder was plausible. However, said technical effect underlying the present application is obvious in the light of the cited prior-art document (1).

- 3.1.4 Finally, the appellant's argument that the side-effects (Guillain-Barré syndrome, which is related to radiculitis) disclosed for zimelidine would have deterred the skilled person from trying sertraline cannot be followed. Although this piece of information was already known and commented in document (1) it did not deter its author from praising the positive results of the clinical studies of sertraline as anti-depressive and from proposing its use for the treatment of panic disorder.

Moreover, results of clinical studies concerning side-effects of different drugs are to be evaluated separately. Zimelidine has a quite different chemical framework than sertraline, which is a tetrahydro-naphtylamine derivative, since zimelidine is 3-(4-bromophenyl)-N,N-dimethyl-3-(3-pyridinyl)-2-propen-1-amine). Moreover, document (3) (introduced by the appellant in appeal proceedings) confirms that Guillain-Barré syndrome is of a rare occurrence (see page 19, left-hand column) and that the results of clinical studies performed so far on 10 healthy volunteers were optimistic as regards side-effects of sertraline (page 20, right-hand column).

3.1.5 Consequently, the set of claims of the main request (sole request) fails for lack of inventive step of the subject-matter of claim 1 (Article 56 EPC 1973).

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar

The Chairman

N. Maslin

U. Oswald