Internal distribution code:

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

Datasheet for the decision of 23 October 2017

Case Number: T 1045/13 - 3.3.01

Application Number: 03759693.9

Publication Number: 1558251

IPC: A61K31/44, A61K38/18, A61P25/24

Language of the proceedings: EN

Title of invention:
METHOD OF TREATMENT OF PSYCHOLOGICAL CONDITIONS BY ADMINISTRATION OF NERVE GROWTH FACTOR

Applicant:
Milkhaus Laboratory, Inc.

Headword:
Nerve growth factor/Milkhaus

Relevant legal provisions:
EPC Art. 83
EPC R. 115(2)
RPBA Art. 15

Keyword:
Sufficiency of disclosure - support by the description (no)

This datasheet is not part of the Decision.
It can be changed at any time and without notice.

Decisions cited:
T 0609/02, T 0394/06, T 0019/90

Catchword:

This datasheet is not part of the Decision.
It can be changed at any time and without notice.

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1045/13 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 23 October 2017

Appellant: (Applicant)	Milkhaus Laboratory, Inc. 70 Elm Street Providence, RI 02903 (US)
Representative:	Walker, Ross Thomson Forresters IP LLP Skygarden Erika-Mann-Strasse 11 80636 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 5 October 2012 refusing European patent application No. 03759693.9 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	A. Lindner
Members:	M. Pregetter
	P. de Heij

Summary of Facts and Submissions

I. The present appeal lies from the decision of the examining division refusing European patent application No. 03 759 693.9, published as WO2004/043462.

II. The following documents are referred to below:

(8) Overstreet et al., Pharmacology, Biochemistry and Behavior, 2010, 94, 553-560

(9) McGeary et al., Neuropeptides, 2011, 45, 317-322

III. The decision under appeal was based on the set of claims filed on 2 May 2007 with letter dated 27 April 2007.

The examining division found that the subject-matter of claims 1 and 15 was not sufficiently disclosed (Article 83 EPC); the application as filed did not provide any theoretical background or any reference to the prior art linking the administration of nerve growth factor (NGF) to any of the disorders defined in claim 1. Although the description as filed contained eleven examples, each of them related to a single patient only and none of them included a control. Also, the examples related to several different conditions. They were thus not suitable evidence that any effect was caused by NGF. The examining division furthermore had reservations relating to the amount of NGF administered in the examples, and fundamental reservations concerning oral administration of a protein-based active agent.

IV. With the statement of grounds of appeal, the appellant (applicant) filed a set of 27 claims.

Claim 1 reads as follows:

"A nerve growth factor (ngf) for use in a method of alleviating symptoms of a psychological condition selected from the group consisting of depression, bi-polar disorders, anxiety disorders, panic attacks, agoraphobia, attention deficit syndrome, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS) the method comprising administering to a subject in need thereof the nerve growth factor in an amount effective to treat one or more symptoms of said psychological condition."

This corresponds to claim 1 on which the examining division based its decision.

V. In a communication pursuant to Article 15(1) RPBA the board informed the appellant that during oral proceedings it intended to construe the claims and discuss the meaning of the terms "alleviating symptoms of a psychological condition". The board said it also intended to assess the examples as filed and to consider their relevance when examining sufficiency of disclosure.

VI. By letter dated 13 October 2017 the appellant withdrew its request for oral proceedings and requested a decision based on the state of the file.

VII. The appellant's arguments, in so far as they are relevant to the present decision, may be summarised as follows:

The application as filed contained detailed background information on the conditions to be treated and on the therapeutic use of nerve growth factor (NGF). The description as filed disclosed eleven examples. These examples related to studies carried out on patients with the claimed symptoms, i.e. related to *in vivo* investigations. The examples showed that NGF had a positive effect on various therapeutical conditions in eleven separate patients.

In its decision the examining division had wrongly disregarded the effects of the eleven examples of the application. There were no facts anywhere that cast doubt on the validity of the studies explained in the examples. The examining division had also queried the dosages and mode of administration in a completely unsupported and unsubstantiated way. The eleven examples of the application as filed confirmed that the symptoms of the therapeutical conditions claimed were effectively treated with NGF. This was also supported by document (8), which concluded that NGF had actions predictive of anti-depressant efficacy with a novel, as yet undetermined, mechanism of action (page 559, second last paragraph). Similar information was given in document (9). In view of the *in vivo* data in the eleven examples of the application as filed, it was not necessary to present *in vitro* experimental data to support plausibility. The underlying principle of the action of NGF and the mode of administration were still not known, but there was proof that it did work. The examining division had applied the wrong principles when coming to its conclusion on sufficiency of disclosure.

In this respect the appellant relied on established case law, and specifically decisions T 609/02, T 394/06 and T 19/90. T 609/02 established that the application had to disclose the suitability of the product to be manufactured for the claimed therapeutic application, and that *in vitro* data might be sufficient if the observed effect reflected such a therapeutic application or if there was a clear and accepted established relationship between the shown physiological activities and the disease. Experimental tests were however required only in the absence of patient data. T 394/06 and T 19/90 stressed that a sufficiency objection could only be raised on the basis of serious doubts substantiated by verifiable facts.

VIII. The appellant's final request was that the decision of the examining division be set aside, and that a patent be granted on the basis of the set of claims filed with the statement of grounds of appeal.

IX. Oral proceedings were held on 23 October 2017. At the end of the oral proceedings the chairman announced the decision.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings before the board took place in the absence of the appellant, who was duly summoned but chose not to attend. According to Rule 115(2) EPC, oral proceedings may continue in the absence of a duly summoned party. Further, pursuant to Article 15(3) RPBA, the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly

summoned, who may then be treated as relying only on its written case. In the present case, this has indeed been specifically requested by the appellant (see point VI above). Hence, the board was in a position to announce a decision at the conclusion of the oral proceedings, in accordance with Article 15(6) RPBA.

3. *Sufficiency of disclosure*

Claim 1 is a second medical use claim worded in accordance with Article 54(5) EPC. Attaining the claimed therapeutic effect is a functional feature of the claim. The application must thus disclose the suitability of the substance or composition for the therapeutic application claimed.

It will now be examined which therapeutic effect is defined by the wording of claim 1, and whether the evidence on file is sufficient to show that the claimed compound is suitable for said therapeutic application.

3.1 *Claim construction*

Claim 1 defines a nerve growth factor for use in a method of alleviating symptoms of psychological conditions selected from a group consisting of depression, bi-polar disorders, anxiety disorders, panic attacks, agoraphobia, attention deficit syndrome, premenstrual dysphoric disorder and premenstrual syndrome.

Claim 1 thus defines a treatment in the form of alleviation of symptoms. The symptoms themselves are not specified. They therefore include all symptoms that arise in the psychological conditions defined in the claims. A study of the description reveals a plethora

of symptoms linked to said conditions (page 1, line 19 to page 12, line 25).

The symptoms range from those - such as anxiety and suicidal thoughts - that are clearly linked to the psychological conditions claimed, to others - such as constipation and headaches - which can also be caused by quite different conditions. There seems to be no link between these symptoms, other than being caused by the various psychological conditions claimed.

The board also notes that claim 1 is not limited to the symptoms specifically mentioned in the description.

The subject-matter of claim 1 is thus extremely broad. To make it plausible that the effect of alleviating all these different symptoms is achieved, support for the treatment of all the psychological conditions defined in claim 1 is necessary.

3.2 *Evidence for effective treatment*

The application as filed does not provide any indication of the principle underlying the relationship between the activity of the pharmaceutically active agent, i.e. the NGF, and the therapeutic effect, i.e. the alleviation of the symptoms of the psychological conditions claimed. The description does not provide any information on the mechanism of action of NGF. No background references are cited that link NGF to the therapeutic effects to be obtained, and no *in vitro* assays are provided to illustrate any such effect. In the complete absence of such information, the experimental evidence on file is of decisive importance.

The experimental evidence consists of eleven examples. Each of these examples describes the treatment of a single patient. Various amounts of NGF are administered for various periods of time. The following conditions are treated:
example I: panic attacks and agoraphobia;
example II: anxiety attacks;
example III: anxiety, panic disorder, and hot flashes;
example IV: depression and anxiety;
example V: clinical depression;
example VI: clinical depression and anxiety;
example VII: depression, irritability, frequent headaches, restless sleep, and hot flashes during the patient's one-week premenstrual cycle; chronic month long anxiety;
example VIII: severe situational anxiety and depression;
example IX: depression and anxiety;
example X: constipation, exacerbated by multiple sclerosis;
example XI: hot flashes and mid-cycle dysphoria.

The examples relate to various conditions, but do not cover all the conditions defined in claim 1. There is no data for example on bi-polar disorders and attention deficit syndrome. Also, only a few of the symptoms disclosed in the description are mentioned in these examples. Consequently, the experimental evidence of these examples cannot provide a full disclosure over the whole scope of claim 1.

Nor do the examples give rise to statistically significant data. Each example relates to a single patient only, contrary to common practice which requires a certain number of patients to be tested under the same conditions in order to allow statistical

analysis of the results. Also, in the absence of a control group, placebo effects cannot be excluded.

To sum up, the appellant has chosen to rely solely on experimental evidence in support of the therapeutic treatment as claimed in claim 1. The experimental evidence on file fails however to provide evidence for the effects claimed. The examples do not cover the whole scope of the claim and do not provide evidence of therapeutic efficacy that meets scientific standards (statistically significant number of patients, control group). Effective treatment of the medical conditions under consideration has thus not been shown.

3.3 Consequently, the board comes to the conclusion that the subject-matter of claim 1 is not sufficiently disclosed (Article 83 EPC).

3.4 In view of that conclusion, it is not necessary to discuss the physico-chemical properties of NGF and its mode of administration.

3.5 *Appellant's further arguments*

3.5.1 *Documents (8) and (9)*

It is established case law that once evidence is available from the patent application as filed, then post-published evidence may be taken into account, but only to back up the findings in the patent application. Post-published evidence cannot establish sufficiency of disclosure on its own.

The board has come to the conclusion that the evidence in the application as filed does not constitute a sufficient disclosure. The contents of post-published

documents (8) and (9) cannot change that finding and therefore need not be discussed.

3.5.2 *Appellant's references to the case law*

The appellant has referred to decisions T 609/02, T 394/06 and T19/90.

The situation leading to T 609/02 differs in several aspects from the case in point. The most important difference is that the description under consideration in T 609/02 provided an explanation - at least a theoretical one - of the mechanism underlying the therapeutic application. T 609/02 is however relevant for the present case in establishing that, where the therapeutic effect is a functional technical feature of the claim, the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application and that evidence filed later cannot be used to remedy a fundamental insufficiency of disclosure.

T 394/06 is also based on a factual situation where there was a theoretical background (the over-expression of CASB7439 transcript in tumours) supported by experimental evidence (example 1 of the description as filed). The present situation differs in that no theoretical explanation of the link between NGF and the symptoms of the psychological conditions claimed has been given. T 394/06 is thus not relevant for the present situation.

The board does not consider T 19/90 to be relevant for the present decision. T 19/90 does not deal with a situation where a therapeutic effect which is a functional technical feature of the claim under

consideration has to be established for the first time. This requires (see above) the present application to disclose the suitability of NGF for the claimed therapeutic application. Such suitability has not been convincingly demonstrated.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated