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**Datasheet for the decision
of 20 February 2013**

Case Number: T 1273/09 - 3.3.04
Application Number: 02753323.1
Publication Number: 1466622
IPC: A61K 39/395, A61P 9/00,
A61P 9/12, C07K 16/28,
C07K 16/26, C07K 16/24,
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Language of the proceedings: EN

Title of invention:

Medicinal agent and method for curing diseases accompanied
with vascular dystonia

Applicant:

Epshtein, Oleg Ilich
Sergeeva, Svetlana Aleksandrovna

Headword:

Homeopathic mixture/EPHSHEIN

Relevant legal provisions:

EPC Art. 83

Keyword:

"Sufficiency of disclosure - no"

Decisions cited:

T 0541/96, T 0442/97, T 0792/00, T 0397/02, T 0609/02,
T 1111/02, T 0058/05, T 1785/06, T 1842/06, T 1329/07,
T 0491/08, T 2281/09, T 1685/10

Catchword:

See points 12 to 13 of the Reasons



Case Number: T 1273/09 - 3.3.04

DECISION
of the Technical Board of Appeal 3.3.04
of 20 February 2013

Appellants:
(Applicants)

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Decision under appeal:

**Decision of the Examining Division of the
European Patent Office posted 3 December 2008
refusing European patent application
No. 02753323.1 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman: C. Rennie-Smith
Members: G. Alt
M. Montrone

Summary of facts and submissions

- I. This is an appeal against the decision of the examining division refusing the European application No. 02 753 323.1 The application was published as EP 1 466 622 in accordance with Article 158(3) EPC 1973. It has the title "Medicinal agent and method for curing diseases accompanied with vascular dystonia". The application claims priority from the Russian application RU 2001135015 which has the filing date of 26 December 2001.
- II. The following documents are referred to in the present decision:
- D3 Physiol. Research, vol. 45, 1996, pages 475-477,
 Zelezna, B. et al.
- D7 Bulletin of Experimental Biology and Medicine,
 vol. 135-136, Suppl. 1, 2003, pages 57-59,
 Markel, A. et al.
- D8 Bulletin of Experimental Biology and Medicine,
 vol. 135-136, Suppl. 1, 2003, pages 62-64,
 Epstein, O. I. et al.
- D9 Report of a study conducted by PharmaHungary,
 2008: "Effects of chronic treatment with test
 materials of OOO "NPF" Materia Medica Holding in a
 rat model of coronary occlusion-induced heart
 failure"

D10 Report of a study conducted at the Lomonosov Moscow State University, 2005: "Analysis of the effect of ultra-low doses of antibodies to AG II receptors on systemic arterial pressure and left ventricular hypertrophy in hypertensive SHR rats"

D11 Antiviral Research, vol. 93 , 2012, pages 219-224, Tarasov, S.A. et al.

III. The examining division refused the application because it considered that the subject-matter of the eight claims of the sole request before it lacked novelty (Article 54 EPC) and that the disclosure of the invention was insufficient (Article 83 EPC).

IV. The reasons given by the examining division in its written decision for its finding of lack of sufficiency of disclosure can be summarized as follows:

The dilutions used in the examples (e.g. C12 + C30 + C200) went beyond the Avogadro limit. Therefore, any medicament based on a C12 or even stronger dilution statistically did not contain a single molecule of the diluted substance and was therefore indistinguishable from its diluent. Therefore, the medicament as such was not sufficiently disclosed and, as a consequence, nor was the claimed treatment.

The therapeutic efficacy of a medicament which did not contain any active ingredient was doubtful. For a medical treatment to be considered as sufficiently disclosed experimental evidence had to be provided showing a therapeutic effect linked to an active ingredient. The examples disclosed in the application

did not include a placebo reference. Therefore, no effect over a placebo control was demonstrated and, consequently, the medical treatment was based on a placebo effect. This failure to demonstrate a reproducible therapeutic effect of an active ingredient was a further reason why the claimed subject-matter contravened the requirements of Article 83 EPC.

The experimental set-up and data provided in post-published documents D7 and D8 were insufficient to attribute a reproducible therapeutic effect to the homeopathic medicaments used. Moreover, even if such an effect had been shown it could not be taken into account in order to overcome a lack of disclosure in the application since sufficiency of disclosure must be satisfied at the effective date of the patent application.

- V. With the statement of the grounds of appeal the applicants (hereinafter "appellants") filed a new main request and an auxiliary request.

- VI. Moreover, documents D9 and D10 were enclosed with the statement of the grounds of appeal. Document D11 was submitted with the appellants' letter of 21 January 2013 in order to show "that the claimed concept actually works".

- VII. The board informed the appellants about its preliminary, non-binding opinion in a communication, namely (i) that the claims of the main and auxiliary request contravened the requirements of Article 123(2) EPC, (ii) that, because the feature or features imparted to the product by the process by which it was defined were not

known, it was also not known by which feature or features the product could be distinguished from known products, and that therefore the claimed subject-matter did not fulfil the clarity-requirement of Article 84 EPC and finally (iii) that the examples in the application were not appropriate to make the treatment according to the claimed second medical use plausible so that the requirements of Article 83 EPC were also not fulfilled.

- VIII. A further (second) auxiliary request was filed in response to the board's communication.

The only claim of the second auxiliary request read:

"1. A mixture of homeopathic dilutions C12 + C30 + C200 of polyclonal rabbit antibodies against the C-terminal fragment of the angiotensin II receptor for use in treating hypertension."

- IX. Oral proceedings were held on 20 February 2013.

The appellants withdrew their main request and first auxiliary request and made the second auxiliary request their new main request.

- X. The appellants arguments, insofar they are relevant for the present decision, may be summarized as follows:

Article 83 EPC

The claimed treatment did not rely on homeopathic concepts of individual prescription and curing similar with similar, but was based on antibodies, a substance

never used in homeopathy, and was grounded on conclusive medicine principles.

The pharmaceutical preparation used in the treatment according to claim 1 was diluted beyond the Avogadro limit.

By multiple consecutive dilution according to homeopathic technology the activity of the original substance was "released" to the diluent so that after the dilutions the diluent had properties which the undiluted diluent did not possess. The way in which the diluent stored and transmitted information needed further study, but it was not contrary to well-established physical laws.

The data of Example 4 from the treatment of a human being diagnosed with "essential hypertension with primary heart involvement, 2nd degree, myocardial hypertrophy of the left ventricle" clearly demonstrated a causal link between the medicament and the effect. Thus, the medicament had an activity and therefore it was not correct to say that the preparation did not contain any active ingredient.

The relevant question in the context of Article 83 EPC and claims to a second medical use was, whether or not the skilled person was enabled to treat the disease - here hypertension.

It was neither required that the effect achieved by a medical preparation had to be based on a tangible **molecule**, nor that the mechanism underlying the therapeutic effect be understood, nor that the data

provided in support of the treatment were statistically relevant, in particular not if the scope of the claim was as narrow as it was here.

Therefore, saying that the data of Example 4 did not make it plausible that the composition referred to in the claim could be used for the treatment of hypertension without any further substantiation as to why, amounted to simply saying "I do not believe them".

Thus, the data in the application demonstrated that the mixture referred to in the claim had a therapeutic effect. That such an effect was present was furthermore derivable from the post-published documents D7 to D11.

Consequently, the application fulfilled the requirements of Article 83 EPC.

Requests

The appellants requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request.

Reasons for the decision

Main request

1. In view of its decision on Article 83 EPC the board has not deemed it necessary to take a decision on whether or not the claimed subject-matter fulfils the requirements of Articles 123(2) and 84 EPC.

Article 83 EPC

2. The only claim of the main request is a claim for a so-called second medical use and reads:

"Mixture of homeopathic dilutions C12 + C30 + C200 of polyclonal rabbit antibodies against the C-terminal fragment of the angiotensin II receptor for use in treating hypertension."

- 2.1 According to the terminology of homeopathic medicine a homeopathic dilution "C" means that one part of a "mother" solution of a substance - here: a solution of polyclonal rabbit antibodies against the C-terminal fragment of the angiotensin II receptor - is added to ninety-nine parts of a diluent, i.e. normally water or alcohol, and subsequently vigorously shaken. One part of this diluted solution is then further diluted in ninety-nine parts of diluent and shaken and so on. For a "C12" dilution twelve dilution steps are performed, thirty are performed for the "C30" dilution and two-hundred for the "C200" dilution. In homeopathic terminology this process of serial dilutions is called "potenisation".

- 2.2 According to homeopathic theory the higher the dilution of a substance is, the stronger its healing effect. Hence, a C200 dilution of a "mother" solution is considered to be more effective than its C12 dilution. Thus, according to homeopathic theory the mixture referred to in claim 1 comprises dilutions of different therapeutic strength.

2.3 It is generally accepted that homeopathic dilutions which are C12 and higher statistically do not contain a single molecule of the substance of the "mother" solution. It was confirmed by the appellants at the oral proceedings that this also applies to the three dilutions of the mixture referred to in the claim, i.e. none of them statistically contains a single antibody molecule.

2.4 According to homeopathic theory the absence of a tangible molecule does not mean that the diluted solution is inactive. Homeopaths consider that by the potentisation process "information" of the substance in the "mother" solution is progressively transferred to the diluent. Also the appellants submitted that due to a "release" of the activity of the original substance to the diluent during the multiple dilutions, the diluent of the dilutions referred to in claim 1 has properties which the undiluted diluent does not have. The appellants contended also that the way in which the diluent stores and transmits the "information" is not known.

2.5 For the sake of the argument the board accepts in favour of the appellants that the mixture referred to in claim 1 contains an active "principle", yet of unknown nature.

3. Treatments according to homeopathic medicine are carried out according to the principle "similia similibus curentur" ("like cures the like"). This means that, if an undiluted substance **causes** particular symptoms in a healthy individual, the same substance, yet given as a homeopathic dilution, can **cure** these

very same symptoms in a sick individual. This approach is different from that relied on for treatments according to "conventional" (allopathic) medicine.

3.1 In the present case the substance in the solution to be diluted according to homeopathic technology is "antibodies against the C-terminal fragment of the angiotensin II receptor".

3.2 It is generally known that the effects mediated by the angiotensin receptor II include vasoconstriction, aldosterone synthesis and secretion, increased vasopressin secretion, cardiac hypertrophy, augmentation of peripheral noradrenergic activity, vascular smooth muscle cells proliferation, decreased renal blood flow, renal renin inhibition, renal tubular sodium reuptake, modulation of central sympathetic nervous system activity, cardiac contractility, central osmocontrol and extracellular matrix formation.

Antibodies binding to the angiotensin receptor II and in particular its C-terminal fragment can block the activation of the receptor. The blockage causes vasodilation, reduces secretion of vasopressin, and reduces production and secretion of aldosterone, amongst other actions. These combined effects **reduce the blood pressure**. Therefore, angiotensin II receptor-binding antibodies have been suggested in the framework of "conventional" medical treatments as agents for the reduction of blood pressure, i.e. for the treatment of **hypertension** (see document D3, page 475, in particular the second paragraph).

- 3.3 Since the "undiluted" antibodies against the C-terminal fragment of the angiotensin II receptor **lower** the blood pressure, the mixture referred to in claim 1, were it to be applied in accordance with homeopathic principles, would have to be used for treating patients suffering from **hypotension**. However, claim 1 requires that the homeopathic mixture is used for treating **hypertension**. Thus, it is applied in accordance with conventional medical principles. This is also admitted by the appellants who state that the treatment is "grounded on conclusive medicine principles".
4. Hence, in the light of the observations in points 2 to 3.3 the board considers that the claimed invention would be perceived as "unusual" (i) from a conventional medical practitioner's point of view because the mixture defined in claim 1 does not achieve the therapeutic effect on the basis of a tangible substance, but on the basis of an unknown "active principle" and (ii) also from a homeopath's point of view because, although being a mixture of homeopathic dilutions, it is not applied in accordance with homeopathic theory. In fact, the claimed invention combines concepts of homeopathic and conventional medicine. There is no document in these proceedings published before the priority date of the application disclosing a treatment relying on this "chimeric" approach.
5. Article 83 EPC stipulates that a European patent application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

As established by the case law of the Boards of Appeal an invention is considered to be sufficiently disclosed in accordance with the provisions of Article 83 EPC, if the disclosure allows it to be performed without undue burden (Case Law of the Boards of Appeal, 6th edition 2010, II.A.4.2).

This has been interpreted by the case law in relation to claims to a second medical use to mean that the skilled person must not only be able to produce the compounds referred to in the claim but that it must also be put in a position by the disclosure in the application in combination with, or by, the common general knowledge to achieve the claimed treatment, i.e. the therapeutical effect, in a reliable and reproducible manner (Case Law of the Boards of Appeal, 6th edition 2010, II.A.4.2, 7th paragraph).

6. The European Patent Convention does not lay down the prerequisites which the disclosure in an application must satisfy to fulfil the requirements of Article 83 EPC. Therefore, as the Boards of Appeal have repeatedly held, whether or not the disclosure is sufficient, is a matter to be decided on the circumstances of each individual case. Ultimately, the disclosure must be such that in its light the examining division or - as the case may be - the board is satisfied that the skilled person can carry out the claimed invention without undue burden (see Case Law of the Boards of Appeal, 6th edition 2010, II.A.5.1.1, 4th and 5th paragraph; II.A.7., last paragraph).

7. Therefore, since in relation to a claim to a second medical use it is required that the disclosure puts the skilled person in the position to achieve the therapeutical effect in a reliable and reproducible manner (see point 5 above), it follows from the observations in point 6 above that - unless this is not already derivable from the prior art - the application must provide suitable evidence in this respect. To this end, any kind of experimental data have been accepted by the Boards. It has also been repeatedly emphasized that "it is not always necessary that results of applying the claimed composition in clinical trials, or at least to animals are reported" (see for example decision T 609/02, point 9 of the Reasons).

8. As observed above in point 4, in the present case the "chimeric" approach disclosed in the present application was not part of the common general knowledge at the priority date of the application. Therefore, whether or not the skilled person is in a position to achieve the claimed treatment of hypertension in a reliable and reproducible manner has to be judged on the disclosure in the application alone. Since the description contains nothing which would allow the skilled person to verify the success of the claimed treatment, the examples are particularly relevant.

9. Examples 1 to 3, 4 to 6 and 8 relate to the treatment of hypertension:
 - 9.1 Examples 1 to 3 disclose experiments with "ISIAH rats with hereditary arterial hypertension".

Example 1 discloses the results of an experiment with 10 animals to which polyclonal rabbit antibodies against the C-terminal fragment of the **human angiotensin II receptor** in a mixture of homeopathic dilutions of **C12 + C30 + C200** were administered.

Example 2 discloses the results of an experiment with 10 rats to which monoclonal antibodies to **angiotensin II** in a mixture of homeopathic dilutions of **C12 + C30 + C200** were administered.

Example 3 discloses the administration to an unknown number of rats of polyclonal mouse antibodies to **angiotensin I** in a mixture of homeopathic dilutions of **D6 + C12 + C200**.

9.2 Examples 4 to 6 and 8 each disclose the results of the treatment of one human being suffering from hypertension for different reasons.

To them

- polyclonal rabbit antibodies against the C-terminal fragment of the **human angiotensin II receptor** in a mixture of homeopathic dilutions of **C12 + C30 + C200** (Example 4);
- a **combination** of **monoclonal** antibodies to **angiotensin II receptor** in a mixture of homeopathic dilutions of **C12 + C30 + C200** and monoclonal antibodies against **angiotensin II** in a mixture of homeopathic dilutions of **D12 + C30 + LM2** (Example 5);

- a **combination** of polyclonal rabbit antibodies against the **angiotensin II receptor** in a mixture of homeopathic dilutions of **C12 + C30 + C200** and monoclonal antibodies against **adrenocorticotropin** in a mixture of homeopathic dilutions of **C12 + C30 + C200** (Example 6); and
- a **combination** of monoclonal antibodies against **tumour necrosis factor alpha** in a mixture of homeopathic dilutions of **C12 + C30 + C200** and antibodies against **tumour necrosis factor alpha receptor** in a mixture of homeopathic dilutions **D12 + LM10** (Example 8),

respectively, was or were administered.

10. In Examples 2 and 3 mixtures of homeopathic dilutions of compounds are tested which are not derived from solutions of polyclonal rabbit antibodies against the C-terminal fragment of the human angiotensin II receptor. In Examples 5, 6 and 8 combinations of mixtures are used, some of which do not even include the mixture according to claim 1. None of these examples relates therefore to embodiments of claim 1 and they are consequently not relevant with regard to the present issue. Thus, only Examples 1 and 4 are relevant.

11. Example 1 discloses a study with rats. The result is summarized as follows:

"The data in the table show that the medication exerts a hypotensive effect".

Example 4 reads as follows:

"Patient D., 50 years old, presented with a 10-year history of essential hypertension. On clinical and instrumental examination, he was diagnosed with "essential hypertension with primary heart involvement, 2nd degree, myocardial hypertrophy of the left ventricle". He was administered polyclonal rabbit antibodies against the C-terminal fragment of the angiotensin II receptor (a mixture of homeopathic dilutions C12 + C30 + C200), 1 tablet BID. The blood pressure stabilized at 130-135 / 85 mm Hg within 7 days of the start of treatment. After 2 months of treatment, electrocardiography revealed a decrease in the myocardial hypertrophy and overload of the left ventricle."

- 11.1 The board notes that neither of these two Examples 1 and 4 includes tests where substances serving as negative controls are applied. Moreover, Example 4 fails, for example, to indicate the initial blood pressure or which measures had been taken to exclude that the hypotensive effect could be due to other reasons, for example other treatments, intake of particular food, increased sport activity, etc.

12. The board has serious doubts that the claimed treatment of hypertension can be reliably and reproducibly achieved by the mixture referred to in claim 1 for the reasons summarized in point 4 above, namely, (i) because on the standards of "conventional" medicine and science it is unconceivable that a homeopathic medicament which does not contain any active substance achieves specific therapeutic effects and (ii) because

on the standards of homeopathic medicine it is unconceivable that a homeopathic medicament that is not applied according to homeopathic principles achieves specific therapeutic effects.

When balancing these factual circumstances against the quality (see point 11.1 above) and quantity (see points 9.1 and 9.2 above) of the relevant evidence in the application, i.e. Examples 1 and 4, the board comes to the conclusion that the level of evidence is not sufficient to satisfy it that the skilled person can reliably and reproducibly achieve the claimed therapeutic effect. Therefore, the board cannot come to the conclusion that the disclosure in the application - and this is the only source of information in the present case (see point 4 above) - puts the skilled person in the position to achieve the claimed treatment of hypertension in a reliable and reproducible manner. Hence, the disclosure of the invention in the application is considered to be insufficient.

12.1 The board observes that the reason for this conclusion is not, as suggested by the appellants' submission (see section X, paragraph 7 above), a mere, unsubstantiated "disbelief". Rather, the conclusion is drawn by taking into account the quality and quantity of available evidence which is considered to be inappropriate in the light of the character of the present invention.

13. The present board's conclusion is in harmony with rulings of Boards of Appeal in a number of cases which it considers to be similar to the present case insofar as in those cases also the boards had serious doubts that the skilled person could achieve the suggested

effect of the claimed invention on the basis of the disclosure in the application or the common general knowledge because, for example, the invention was conceptually new, went against prevailing opinion or established theories, was in an unexplored field or appeared to go against natural laws and therefore have called for a particularly conclusive disclosure of the invention (see for example decisions T 541/96, points 5 to 8 of the Reasons; T 442/97, points 3.2, 3.14 and 3.15 of the Reasons; T 792/00, points 3, 4, 7 and 11 of the Reasons; T 397/02, points 12, 16 and 18, ; T 1111/02, points 8 and 12 of the Reasons; T 58/05, points 2.3 and 2.4 of the Reasons; T 1785/06, points 3.4.1 to 3.4.3 of the Reasons; T 1842/06, points 3.1 to 5.4.4 of the Reasons; T 1329/07, points 2.2.1 to 2.2.5 of the Reasons; T 491/08, points 6 to 12 of the Reasons; T 2281/09, points 2.1, 2.4, 2.8 and 2.9; T 1685/10, points 3.1 to 3.8 of the Reasons).

14. Sufficiency of disclosure must be satisfied at the effective date of the patent, i.e. on the basis of the information in the patent application together with, or on the basis of, the common general knowledge then available to the skilled person. Therefore, the disclosure in post-published documents can only be taken into account for the question of sufficiency of disclosure if it was used to back up the positive findings in relation to the disclosure in a patent application (see for example decision T 609/02, point 8 of the Reasons). Thus, in view of the board's conclusion in point 12 above, none of documents D7 to D11 can therefore be taken into account here.

15. The application does not fulfil the requirements of Article 83 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

P. Cremona

C. Rennie-Smith