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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DIETER CULLMANN and GUNTHER BURGARD

Appeal 2017-004107
Application 12/578,354
Technology Center 1600

Before DEMETRA J. MILLS, ERIC B. GRIMES, and ELIZABETH A. LAVIER, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF CASE

The following claim is representative.

17. A method of treating arterial hypertension in a mammalian individual having chronically elevated blood pressure, the method comprising administering to the individual hyaluronidase in an amount of at least 3,000 IU of hyaluronidase per day.

Cited References

Winn	US 5,250,548	Oct. 5, 1993
Burgard	US 2005/0249717 A1	Nov. 10, 2005

J. J. Ryan, *The Treatment of Hypertension by Hyaluronidase*, Milne Pub., 132–42 (1954).

O.S. Gilyova et al., *The Achievements of Modern Medicine in Systemic Hirudotherapy*, Russian Journal of Biomechanics, Vol. 3, No. 4, 1–10 (1999).

Hana Rauchova et al., *The Effect of Chronic L-carnitine Treatment on Blood Pressure and Plasma Lipids in Spontaneously Hypertensive Rats*, European Journal of Pharm., Vol. 342, 235–39 (1998).

Jorge Martins de Oliveira, et al., *Intravenous Injection of Hyaluronidase in Acute Myocardial Infarction: Preliminary Report of Clinical and Experimental Observations*, Am. Heart J., Vol. 57, No. 5, 712–22 (1959).

Grounds of Rejection

Claims 39, 40, and 42 stand rejected under 35 U.S.C. § 112(a) or 35 U.S.C. § 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement.

Claims 17–21, 23–27, 31, and 39–46 stand rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Ryan taken with Gilyova, de Oliviera, and Burgard, and further taken with Rauchova and Winn.

FINDINGS OF FACT

The Examiner's findings of fact are set forth in the Answer at pages 2–7.

PRINCIPLES OF LAW

In making our determination, we apply the preponderance of the evidence standard. *See, e.g., Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1427 (Fed. Cir. 1988) (explaining the general evidentiary standard for proceedings before the Office).

"[O]bviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

Written Description

The Examiner finds that

> no clear basis or support is found in this section of the written disclosure for the invention as now claimed because there is no correlation between the material disclosed and the claimed reduction in blood pressure. The portion of the Specification cited does not indicate a dosage or regimen of administration of hyaluronidase with any specificity. The functional limitations argued are not specific as to any particular reduction in blood pressure due to particular amounts of hyaluronidase. Similarly, the cited portions at page 10 to page 11 are not specific as to results to be obtained.

Ans. 3.

In particular,

> regarding the working examples, it is noted that any results provided in the as-filed specification wherein a reduction in blood pressure is specifically indicated require the

> administration of at least 4500 IU hyaluronidase. No results are shown for the range of 3000 to 4500, for example. The exemplified material does not provide sufficient support for the new generic recitation of reducing diastolic blood pressure in the individual by at least 5 mm Hg, respectively at least 10 mm Hg and/or to reduce systolic blood pressure in the individual by at least 5 mm Hg, respectively at least 10 mm Hg by administering at least 3000 IU hyaluronidase per day, for one day, for example.

Ans. 3.

Appellants state that support for the claims is found at page 10, line 32 to page 11, line 3 of the Specification. App. Br. 5.

We find that the Examiner has not set forth a prima facie case of lack of written description. Appellants point to pages 10 and 11 of the Specification, which state in several locations that "[a]ccording to a preferred embodiment, at least about 3,000 IU … of hyaluronidase are administered per day." The Specification also describes "using hyaluronidase for the prevention and/or treatment of arterial hypertension." Spec. 2. Thus, the Specification, on its face, describes the administration of 3,000 IU of hyaluronidase per day to treat arterial hypertension. As the Federal Circuit has noted:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.

Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006) (quoting *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005)).

The written description rejection is reversed.

Obviousness Rejection

The Examiner finds that Ryan teaches the treatment or prevention of chronic hypertension, including arterial hypertension and secondary hypertension by administering an effective amount of hyaluronidase. *See, e.g.*, Ryan pages 132–39. Final Act. 4.

In addition, the Examiner finds that

> Gilyova et al. teach the treatment of hypertension or "chronically elevated blood pressure" with hyaluronidase, since it discloses the treatment of hypertension with leeches, which contain hyaluronidase. *See, e.g.*, Gilyova et al., page 2, paragraph 3 and Specification, page 8, paragraph 1, the effectiveness of the treatment of hyaluronidase on hypertension is disclosed at Gilyova et al. page 3, paragraphs 4 and 7 et seq.

Final Act. 4.

> It is also noted that in the process of treatment of Gilyova *et al.,* while the patients are clearly suffering from hypertension, other patients having cardiovascular disease are treated in a similar manner, which strongly suggests that similar or related mechanisms are involved in hypertension and other manifestations of cardiovascular disease and the effectiveness of medicaments, including hyaluronidase, in the treatment of these related conditions was known in the art at the time the claimed invention was made.
>
> In addition, De Oliveira *et al.* teach a method of treating arterial hypertension by administering to an individual an effective amount of hyaluronidase. See, e.g., Case Reports on

patients pages 714, first paragraph and Burgard *et al.* teach a method of treating arterial hypertension by administering to an individual an effective amount of hyaluronidase. See, e.g., [0026]. See paragraphs [0026]-[0028] for administration protocols.

The administration of hyaluronidase in combination with the antihypertensive agent carnitine is disclosed at [0029] in Burgard *et al.* In this regard, Rauchova *et al.* adequately demonstrates that carnitine is an antihypertensive agent. See, e.g., page 237, first full paragraph. In addition, Winn *et al.* disclose the administration of various antihypertensive agents together with agents such as diuretics, vasodilators, adrenergic blocking agents, calcium channel blockers, angiotensin converting enzyme inhibitors, renin inhibitors, etc .. See, e.g., col. 191, line 19 et. seq.

Final Act. 5.

1) Appellants submit that there is no evidence in Ryan that hyaluronidase treated hypertension in any of the patients discussed therein. One cannot conclude, from the disclosure of Ryan, that hyaluronidase treats hypertension. App. Br. 9.
2) Appellants argue that a close reading of Ryan does not show that hyaluronidase treated hypertension in any of the patients. App. Br. 9.
3) Appellants submit that Ryan does not provide sufficient guidance for one of ordinary skill in the art to use an amount of hyaluronidase administered per day of at least 3,000 IU to treat arterial hypertension. App. Br. 11.
4) Appellants argue that Gilyova discusses application of leeches to provide a variety of effects, including anti-thrombal, anti-aggregative, thrombolytic, anti-inflammatory, anti-ischemic,

analgesic, vasodilative, and hypotensive effects (Gilyova, page 3, paragraph 4). However, Appellants submit that there is no disclosure in Gilyova of the use of hyaluronidase to treat arterial hypertension. App. Br. 12.

5) Appellants argue that one of ordinary skill in the art would not attribute to hyaluronidase the antihypertensive effect of hirudotherapy, and Gilyova fails to disclose or suggest the treatment of hypertension with hyaluronidase. App. Br. 13.
6) With respect to de Oliveira, Appellants argue that the patient referred to on page 714 did not suffer from an arterial hypertension as alleged in the Office Action. Instead, the patient was suffering from a diaphragmatic infarction as shown and commented in de Oliveira with Figure 4 (page 715). Figure 4 of de Oliveira reads: "Acute diaphragmatic infarction extending to the dorsal regions." App. Br. 14.
7) Appellants argue that Burgard indicates that the treatment is for cardiac hypertrophy and fatty disease of the heart, and for reducing the risk of infarction, and argue that Burgard does not mention treating arterial hypertension. App. Br. 15.

ANALYSIS

We do not find that the Examiner has provided evidence to support a prima facie case of obviousness. In particular, the Examiner has failed to provide evidence in the prior art of the treatment of hypertension with hyaluronidase in the dosage claimed.

We begin with claim interpretation. Appellants' Specification states that:

> hyaluronidase is used for the treatment of an arterial hypertension selected from the group consisting of endocrine hypertension, essential hypertension, arteriosclerotic hypertension, cardiovascular hypertension, *renal hypertension*, labile hypertension, neurogenic hypertension, paroxysmal hypertension, portal hypertension, pulmonary hypertension, and *secondary hypertension*. Also encompassed by "arterial hypertension" as used herein is a hypertension caused by monogenic defects such as glucocorticoid-remediable aldosteronism and Liddle's syndrome, hypertension caused by hypertension-susceptilibity [sic] genes such as angiotensinogen and alpha-adducin genes. "Arterial hypertension" according to the invention may as well be caused by environmental factors such as salt intake, preferably sodium intake, obesity, occupation, and alcohol intake, all of which forms of hypertension are also contemplated as being encompassed by the present invention. Moreover, hypertension in the sense of the present application also includes hypertension caused by obstructive sleep apnea, by aortic coarctation, *by preeclampsia*, by drugs such as combined oral contraceptive pill, cyclosporin, steroids, and by CNS disturbances.

Spec. 5 (emphases added). Appellants' Specification also states that, "there is no correlation between the amount of plaques or sclerotified vessels and the occurrence of hypertension." Spec. 2. Appellants note that, "[t]his is also consistent with the finding that as a result of the Hyaluronidase treatment the present inventors observed a sustained and significant reduction in arterial hypertension in hypertensive patients who displayed no significant arteriosclerotic plaques before and after commencement of the Hyaluronidase treatment." Spec. 3.

While claim 17 describes treatment of arterial hypertension, claim 18 further defines arterial hypertension to include, "endocrine hypertension,

essential hypertension, arteriosclerotic hypertension, cardiovascular hypertension, renal hypertension, labile hypertension, neurogenic hypertension, paroxysmal hypertension, portal hypertension, pulmonary hypertension, or secondary hypertension." Thus, by the doctrine of claim differentiation, claim 17 encompasses the conditions of claim 18. In other words, "arterial hypertension" includes renal hypertension and secondary hypertension.

As to Ryan, we agree with Appellants that Ryan does not teach the claimed dosage of hyaluronidase. While Ryan arguably teaches treatment of secondary hypertension associated with a kidney infection, or pregnancy preeclampsia hypertension within the scope of the pending claims, we agree with Appellants that the evidence of the effectiveness of hyaluronidase in treating hypertension in Ryan may have been inconclusive to one of ordinary skill in the art at the time of the invention. Several treatment groups in Ryan's studies, Group IV in particular, did not respond to the treatment or were made worse by the hyaluronidase treatment. App. Br. 9–10.

We agree with Appellants that Gilyova is inconclusive with respect to hyaluronidase effectiveness in treating hypertension, because hyaluronidase is but one of many substances present in leech saliva that could be responsible for the hypertension reduction effects. App. Br. 12.

The patients discussed in de Oliveira are restricted to those exhibiting acute myocardial infarction. App. Br. 14. The Examiner has failed to point to any specific disclosure in de Oliveira that its treatment protocol had any effect on blood pressure. *Id.* We further note that there is no evidence that the de Oliveira patient with atherosclerosis is an individual within the scope of the pending claims (i.e., an "individual having chronically elevated blood

pressure"), as Appellants' Specification establishes that "there is no correlation between the amount of plaques or sclerotified vessels and the occurrence of hypertension." Spec. 2.

With respect to Burgard, the Examiner argues generally that Burgard treats a form of heart disease which includes hypertension. Ans. 5. However, the claim scope is limited to treating arterial hypertension in a mammal with a specific dosage of hyaluronidase. We find that the Examiner has failed to establish that the forms of heart disease mentioned in Burgard encompass arterial hypertension.

We do not reach Appellants' proffered evidence of unexpected results because we find that, in the first instance, the Examiner has failed to establish a prima facie case of obviousness on the evidence before us.

The obviousness rejection is reversed.

CONCLUSION OF LAW

The cited references do not support the Examiner's obviousness rejection, which is reversed. The written description rejection is also reversed.

REVERSED