

The opinion in support of the decision being entered today was not written for publication and is not precedent of the Board.

Paper No. 19

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte VICTORIA M. KNEPP,
DEBORAH M. LIDGATE, RICHARD MASKIEWICZ
and LEO GU SARATOGA

Appeal No. 1997-2356
Application 08/109,798

ON BRIEF

Before WINTERS, MILLS, and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 1-11, which are all of the claims pending in this application.

We reverse.

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Claim 1 is illustrative of the claims on appeal and reads as follows:

1. An aqueous pharmaceutical formulation comprising: (a) biologically active nerve growth factor; (b) biologically acceptable salt in an amount sufficient to maintain isotonicity; (c) a buffer in an amount sufficient to maintain the pH of the formulation from about 4.5 to about 6.0; and (d) water.

The prior art references relied upon by the examiner are:

Finkenaur et al. (Finkenaur) EP 0 308 238 March 22, 1989

Pignatti et al. (Pignatti) "Solution Properties of \$ Nerve Growth Factor Protein and Some of Its Derivatives," Journal of Neurochem., Vol. 25, pp. 155-159 (1975)

Wang et al. (Wang) "Parenteral Formulations of Proteins and Peptides: Stability and Stabilizer," Journal of Parenteral Science and Technology Vol. 42, pp 271-273 (1970)

Diem et al. (Diem) Scientific Tables 7th ed., pp. 271-273, 280-281 and 528-529 (1970)

OPINION

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims, to the applied prior art references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the above-noted rejection, we make reference to the examiner's Answer (Paper No. 18, August 19, 1996) for the examiner's complete reasoning in support of the rejection, and to the appellants' Brief (Paper No. 17, April 18, 1996) for the

appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

DECISION ON APPEAL

35 U.S.C. § 103

Claims 1-11 stand rejected under 35 U.S.C. § 103 as obvious over Finkenaur in view of Pignatti, Wang and Diem.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). An obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

In the present case, Finkenaur is relied on for establishing aqueous, stabilized formulations containing growth factors, such as epidermal growth factor (EGF) and nerve growth factor (NGF). Finkenaur, page 2, lines 36-55. The formulations may include water

soluble extenders or carriers which may include tricarboxylic and dicarboxylic acids (e.g. citric acid and tartaric acid) and inorganic salts, such as sodium or potassium phosphate. The water content of the lyophilized composition is preferred to be less than 1% but may be as high as 5%. Answer, page 5. The pH of the growth factor formulations described by Finkenaur may be between 5 and 8. Finkenaur, page 5, lines 5-6. In one particular growth factor formulation, sodium chloride is used as a tonicity agent. Finkenaur, example 1, page 6. Thus Finkenaur provides general evidence of a formulation comprising nerve growth factor, biologically acceptable salts, buffers providing the claimed pH range and water. The specific examples of Finkenaur, however, appear to be directed to EGF formulations.

The examiner relies on Pignatti for establishing an acceptable pH range for NGF of 4.0 to 10. Pignatti, Table I, page 157, Figure 1. More particularly, Pignatti discloses NGF is biologically active and does not aggregate in a pH range of 4.0 to 7.6, which overlaps the claimed pH range of 4.5 to 6.0. Pignatti, Table I, page 157, Figure 1.

Wang is relied on by the examiner primarily for establishing that serum albumin is a known stabilizer for enzymes. Answer, page 7. Diem is indicated by the examiner to establish the concentration of NaCl in normal saline of 0.85%. Diem additionally discloses that sodium citrate/HCl has buffering capacity in the range of 1.2 to 5.0 and that

citric acid/phosphate buffers have a buffering capacity in the range of 2.2-7.8. Answer, page 7.

It is the examiner's position that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to provide NGF in an aqueous pharmaceutical composition or formulation at the concentrations, and with biologically compatible buffers and carriers as taught by Finkenaur, at a pH of about 5.0 as taught by Pignatti, using a stabilizer such as human serum albumin, as taught by Wang, and using isotonically normal salt concentrations and citric acid as taught by Diem, so that the NGF may be used in a pharmaceutical formulation that will provide the stable and biologically active NGF for pharmaceutical use due to the known benefit of NGF on neurons, as taught by the references. Answer, pages 7-8.

Where the prior art, as here, gives reason or motivation to make the claimed NGF formulation, the burden then falls on an appellants to rebut that prima facie case. Such rebuttal or argument can consist of any other argument or presentation of evidence that is pertinent. In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991).

In the present case, appellants rely on a Declaration of Deborah Lidgate as evidence of the nonobviousness of claimed invention. The appellants argue that the Lidgate Declaration provides experimental results of the improved stability of NGF in the

pH range of 4.5 to 6.0 and argue that this result is unexpected and highly material to the production of stable NGF. Brief, page 4. Appellants' position is that, absent factual evidence to the contrary, the examiner is not entitled to discount the Lidgate Declaration arguments and evidence.

In our view, the examiner has not provided factual evidence and argument to the contrary, indicating that NGF shows unexpected stability in the claimed pH range of 4.5 to 6.0. The examiner's main argument appears to be that the Declaration does not provide an adequate presentation of data. On this basis, the examiner finds that the conclusions set forth in the Lidgate Declaration regarding the stability of NGF in the claimed pH range cannot be considered unexpected in view of the teachings of Pignatti of biologically active NGF within the claimed pH range. Answer, page 11.

To the contrary, we find that the Lidgate Declaration data has probative value and provides adequate evidence of unexpected stability of NGF in the pH range of 4.5 to 6.0 which is sufficient to rebut the examiner's prima facie case of obviousness. "[A] prima facie case of obviousness based on overlapping ranges can be rebutted if the applicant (1) can establish 'the existence of unexpected properties in the range claimed' or (2) can show 'that the art in any material respect taught away' from the claimed invention." In re Geisler, 116 F.3d 1465, 1468, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997) (quoting In re Malagari, 499 F.2d 1297, 1303, 182 USPQ 549, 553 (CCPA 1974)). Moreover, neither

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the board nor an examiner can substitute its judgment of the Lidgate Declaration for that of an established expert in the art. In re Zeidler, 682 F.2d 961, 965, 215 USPQ 490, 494 (CCPA 1982).

Although Pignatti appears to describe an absence of aggregation and a biologically active NGF in the pH range of 4.0 to 7.6 (Table 1, page 157), the examiner has not shown that Pignatti describes or suggests the unexpected stability of NGF in the pH range of 4.5 to 6.0 as evidenced by the reduced rate of degradation for NGF in that range. Lidgate Declaration, Exhibit 1.

After evidence or arguments are submitted by the appellants in response to rejection based on obviousness, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of the argument. We have carefully studied the arguments and evidence of record. On balance, we believe that the totality of the evidence presented by the examiner and appellants weighs in favor of finding the claimed invention not to be obvious in view of the cited references. The rejection of the claims for obviousness of the claimed invention is reversed.

CONCLUSION

The rejection of claims 1 -11 under 35 U.S.C. § 103 is reversed.

REVERSED.

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No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

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