

The opinion in support of the decision being entered today is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte RENE BELDER and MARK E. MCGOVERN

Appeal 2007-0185
Application 10/305,281
Technology Center 1600

Decided: June 28, 2007

Before DONALD E. ADAMS, DEMETRA J. MILLS, RICHARD M. LEBOVITZ,
Administrative Patent Judges.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

The Appellants appeal the Examiner's final rejection of claims 1-9 for obviousness.

We have jurisdiction under 35 U.S.C. § 6(b) (2002).

WE AFFIRM.

Claim 1 is directed to:

1. A method for reducing LDL cholesterol levels in an mammal which consists essentially of the administration of 80 mg or 160 mg once per day of pravastatin, or a pharmaceutically acceptable salt or ester thereof, to a mammal in need of such treatment.

Grounds of Rejection

1. Claims 1-9 stand rejected under 35 U.S.C. § 103 over Sherwood.
2. Claims 1-9 stand rejected under 35 U.S.C. § 103 over Joshi.

References cited

Joshi	US 5,030,447	Jul. 9, 1991
Sherwood	GB 2 23 787	Sep. 23, 1992

DISCUSSION

Obviousness - Sherwood

Claims 1-9 stand rejected under 35 U.S.C. § 103 over Sherwood (Answer 4).

The Examiner contends that Sherwood teaches a method of treating hypercholesterolemia comprising the administration of 1-80 mg of LDL-cholesterol lowering amounts of HMG-CoA reductase inhibitors, such as pravastatin, with Chromium (III) in a single or divided dose. (Answer 4.) The Examiner acknowledges that Sherwood does not expressly teach administering 160 mg of pravastatin, and does not particularly teach a composition containing 80 or 160 mg of pravastatin with chromium (III). (*Id.*) However, the Examiner concludes that it would have been obvious to one of ordinary skill in the art to employ the claimed amount of pravastatin in the method and composition of the invention because it is optimization of a result effective parameter. (*Id.*)

Appellants contend that the claim language "consisting essentially of" in claim 1 excludes other active agents such as chromium (III). (Br.¹ 5.) Appellants argue that should a chromium (III) compound be added to Appellants' inventive formulation, it would cause an increase in HDL cholesterol, and result in a material change the inventive concept of the claimed invention. (Br. 14.)

We are not persuaded by Appellants' arguments. Upon review of the Specification, it becomes clear that the object of Appellants' claimed invention is to provide a method for reducing LDL cholesterol levels by administering specific dosages of pravastatin (e.g., Specification 2: 1-10). Thus, the basic and novel characteristics of Appellants' invention is the administration of specific dosages of pravastatin to reduce LDL cholesterol.

Appellants do not define the term "consisting essentially of" in the Specification in any particular manner. Furthermore, Appellants' Specification indicates at page 2, that in order to achieve the objects of their invention, the composition may also include additional active agents. (Specification 2: 15-22.) We do not find that Appellants' claims exclude additional active agents such as chromium III which is added in Sherwood to increase HDL cholesterol levels. Sherwood does not indicate that chromium III has an effect on LDL cholesterol levels. Thus, the addition of chromium III does not readily appear to affect the basic and novel characteristics of Appellants' invention, LDL cholesterol lowering with pravastatin.

Appellants further contend that once daily dosage of 80 and 160 mg of pravastatin without other components, surprisingly and unexpectedly reduced levels of LDL cholesterol to a substantially and significantly greater degree than

¹ Throughout this decision, reference to the Brief, refers to Appellants' Substitute Brief, filed Oct. 8, 2005.

10, 20 or 40 mg of pravastatin. (Br. 6.) This argument of Appellants is unsupported by evidence of record. Appellants have provided no evidence that 80 mg of pravastatin alone lowers LDL cholesterol levels to a greater degree than 80 mg pravastatin and chromium.

Appellants argue that based on the dose response curve (Br. 20), corresponding to example 1, one of ordinary skill in the art would expect that as a once daily dosage of pravastatin is increased beyond 40 mg, the percentage reduction in LDL-cholesterol cholesterol would not be significantly better than that obtained using 40 mg of pravastatin. (Br. 12.)

Appellants thus rely on data from the Physician's Desk Reference (PDR) 54th, edition (2002) page 846 edition, and 2002 PDR, pages 1-23, as evidence of unexpected results and of non-obviousness of the claimed invention.² A characterization of Table 3 of the PDR 2002 is reproduced at page 7 of the Brief and incorporated into the standard dose response curve on page 20 of the Brief. The data from the PDR is indicated in the Brief to reflect the mean percentage reduction in LDL cholesterol from baseline. In contrast, Appellants' Data from Specification, example 1, appears in two forms, an LDL-C actual and LDL-C calculated. A mean percentage reduction in LDL-C was calculated. (Specification 9-10.)

The Examiner finds several deficiencies with Appellants' evidence of unexpected results. (Answer 8.) The Examiner finds that the scale of the x-axis is not "proportional" and that there is a perception of unexpected results appears significant at the higher dosages.

In particular, the Examiner argues

² Pages 1-23 were not attached to the PTO Copy of the Supplemental Brief. Nor does the scanned record reflect they were attached to previous amendments.

When the x-axis of the graph gets shortened and the y-axis stays the same, the slope of the curve will inevitably getting [sic] steeper. When the x-axis is proportional in normal scale and not in log scale, the "steep" increase of the slope would be disappeared. When employing 80mg and 160mg, the LDL reduction are 37% and 45% respectively. When employing 40mg of pravastatin, the LDL reduction is 34%. It is clear that the increase is not really significant because by increasing the dosage by 4-fold (40mg to 160mg), the increase in LDL reduction is only better by about 10%. By doubling the dose, the increase in LDL reduction is only by 3%. Therefore, the alleged "substantial" benefit is actually considered as an expected benefit.

(Answer 8.)

The Examiner also notes that the duration of the trials were different, one being 6 wks and one being 8 wks. (Answer 8-9.)

We agree with the Examiner that discrepancies in Appellants' data exist. The Examiner noted that the PDR and Appellants' data differs by 5% for the same dosage amount, 40 mg. (Answer 13.) Furthermore, it is unclear from Appellants' data whether missing data points at 60, 100, 120, and 140 mg would have resulted in a linear data progression, evidencing an expected decrease in LDL-C. (*Id.*) The Examiner further argues there is no statistical error measurement in the results Appellants have provided, and thus, a determination of statistical significance of the results cannot be made. (*Id.*) While we do not entirely agree with the Examiner's statements that Appellants' data is not statistically significant,³ we do not find on the evidence of record that Appellants have addressed, explained, or resolved the indicated discrepancies in the data they rely upon to show unexpected results.

³ Note "SD" or standard deviation, (Specification 9) and "p-value" (Specification 10).

It is well settled that there must be “clear and convincing evidence” of unobvious results in order to overcome a *prima facie* case of obviousness. *In re Lohr*, 317 F.2d 388, 392, 137 USPQ 548, 550-51 (CCPA 1963). In addition, the presentation of objective evidence of nonobviousness does not, in and of itself, mandate a conclusion of nonobviousness. The fact finder here, the Examiner, is entitled to his own ideas, within reason, as to what evidentiary facts will persuade him of unexpected results. Thus, whether the rebuttal evidence is sufficient to persuade the Examiner is an evidentiary matter left, within reason, to the trier of fact. *In re Johnson*, 747 F.2d 1456, 1460, 223 USPQ 1260, 1263 (Fed. Cir. 1984). We do not find Appellants’ evidence presented in the graph of Example 1, to be fully comparative and thus Appellants’ evidence does not mandate a conclusion of nonobviousness.

While “discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art,” *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980), our reviewing court has found an exception to this general rule where “the parameter optimized was not recognized to be a result-effective variable,” *In re Antonie*, 559 F.2d 618, 620, 195 USPQ 6, 8-9 (CCPA 1977). It is clear from appellant’s data, that the result of lowering cholesterol is dependent upon the amount of pravastatin administered. However, we agree with the Examiner that the data before us indicates that one of ordinary skill in the art would have recognized that when the amount of pravastatin is increased, the expected benefit would be a further reduction in cholesterol levels. As indicated herein, we do not find Appellants’ data convincingly overcomes the Examiner’s *prima facie* case of obviousness.

In view of the above data discrepancies noted by the Examiner, we affirm the Examiner’s *prima facie* case of obviousness.

Obviousness - Joshi

Claims 1-9 stand rejected under 35 U.S.C. § 103 over Joshi (Answer 4).

The Examiner contends that Joshi teaches a tablet composition employing 3 to 50% pravastatin and teaches that the tablet can be up to 1 gm in size. (Answer 5; Joshi, col. 2, l. 65 to col. 3, l. 4; col. 3, ll. 16-17.) The Examiner acknowledges that Joshi does not particularly teach 80 and 160 mg of pravastatin in a tablet. The Examiner concludes however, that one of ordinary skill in the art would have been motivated to incorporate 80 and 160 mg of pravastatin into the composition of Joshi, and that it is obvious to optimize such a dosage. (Answer 5.)

Appellants acknowledge

Joshi et al. disclose a pharmaceutical composition which may contain from about 1 to about 60% pravastatin (preferably from about 3 to about 50% pravastatin) which composition may be in the form of tablets up to 1 gram in size. Thus, a 1 gram tablet would contain 10 to 600 mg pravastatin, preferably 30 to 500 mg pravastatin.

(Br. 9.) Appellants, however, argue that the upper limit of medicament actually shown in Joshi et al. is 40 mg, and that one of ordinary skill in the art would not have been motivated to employ higher dosages of pravastatin. (*Id.*)

We disagree. We find that a person of ordinary skill in the art, at the time the invention was made, would have found it obvious to optimize the amount of drug in a tablet to treat the claimed condition. A minor modification of the prior art, such as optimizing the amount of a particular ingredient, does not distinguish the claimed product from the prior art. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1731, 82 USPQ2d 1385, 1396 (2007) (It is proper to “take account of the inferences and creative steps that a person of ordinary skill in the art would employ.”). *See also id.* at 1742, 82 USPQ2d at 1397 (“A person of ordinary skill is

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also a person of ordinary creativity, not an automaton.”). As set forth in *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955), “[I]t is not inventive to discover the optimum or workable ranges by routine experimentation.” In addition, in at least one case the Federal Circuit has held that the experimentation needed to arrive at a drug dosage “was nothing more than routine.” *Merck v. Biocraft*, 874 F.2d 804, 808, 10 USPQ2d. 1843, 1847 (Fed. Cir. 1989).

In view of the above, the rejection of the claims for obviousness in view of Joshi is affirmed.

CONCLUSION

The rejection of claims 1-9 under 35 U.S.C. § 103 over Sherwood is affirmed. The rejection of claims 1-9 under 35 U.S.C. § 103 over Joshi is affirmed.

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

AFFIRMED

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