

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MONTY KRIEGER,
ANNE BRAUN and HELENA E. MIETTINEN

Appeal No. 2006-1993
Application No. 10/147,651

HEARD: August 8, 2006

Before ADAMS, MILLS, and GREEN, Administrative Patent Judges.

GREEN, 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 1-8 and 10-16. Claims 1 and 13 are representative of the claims on appeal, and read as follows:

1. A method for identifying compounds for treating or preventing atherosclerosis or cardiovascular disease comprising administering compounds that may have an effect on disorders selected from the group consisting of cardiac fibrosis, myocardial infarction, defects in electrical conductance, atherosclerosis, unstable plaque, and stroke to a mouse having decreased expression of active SR-BI and Apo-E wherein the mouse develops atherosclerotic plaque in the aortic sinuses and progressive heart block and

determining the effect of the compound on cardiac fibrosis, myocardial infarction, defects in electrical conductance, atherosclerosis, unstable plaque, stroke, diseases associated with abnormal cardiac structure or function or elevated cholesterol or lipoprotein levels in the mouse relative to control mice not treated with compound.

13. A method for treating or preventing a disorder or disease other than atherosclerosis characterized by abnormal lipoprotein and cholesterol metabolism, wherein the disease is mediated by SR-BI comprising administering to an individual in need thereof a compound selected from the group consisting of 4,4'-(isopropylidenedithio) bis(2,6-di-tert-butylphenol), monoesters and other derivatives thereof, 2,3-Dihydro-5-hydroxy-2,2-dipentyl-4,6-di-tert-butyl-benzofuran or a derivative thereof, vitamin E and vitamin C, wherein the compound is administered in an amount effective to decrease lipoprotein levels or normalize lipoprotein structure or reduce abnormal cholesterol metabolism.

Claims 1-8 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification fails to enable the full scope of the claimed invention. In addition, claims 13, 15 and 16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Baldassarre,¹ and claims 13-16² stand rejected under 35 U.S.C. § 102(b) as being anticipated by Azen.³ Finally, claims 1-8 and 10-12 are subject to an obviousness-type double patenting rejection

¹ Baldassarre et al. (Baldassarre), "Clinical Evaluation of Probucol in Hypercholesterolemia: Individual Lipoprotein Responses and Inhibitory Effect on Carotid Atherosclerosis Progression," Journal of Cardiovascular Pharmacology, Vol. 30, pp. 784-89 (1997).

² The statement of the rejection states that claims 14-16 stand rejected over Azen, see Examiner's Answer, page 6, but as all of those claims depend on claim 13, we assume that claim 13 also stands rejected. That also appears to be the understanding of appellants. See Appeal Brief, page 15.

³ Azen et al. (Azen), "Effect of Supplementary Antioxidant Vitamin Intake on Carotid Arterial Wall Intima-Media Thickness in a Controlled Clinical Trial of Cholesterol Lowering," Circulation, Vol. 94, pp. 2369-72 (1996).

over claims 1-9 of U.S. Patent No. 6,437,215. See Final Rejection, mailed March 16, 2005, page 2. After careful review of the record and consideration of the issues before us, we reverse the rejections under 35 U.S.C. § 112, first paragraph, and under 35 U.S.C. § 102(b). Because appellants do not contest the obviousness-type double patenting rejection, see Appeal Brief, page 18, that rejection is summarily affirmed. Finally, we raise other issues that the examiner may wish to address upon return of the application.

BACKGROUND

“The present invention is generally in the area of transgenic animal models of atherosclerosis, methods for screening for inhibitors acting via interaction with the SR-BI scavenger receptor, and compositions obtained thereby.” Specification, page 1. “SR-BI might play a major role in transfer of cholesterol from peripheral tissues, via HDL, into the liver and steroidogenic tissues, and that increased or decreased expression in the liver or other tissues may be useful in regulating uptake of cholesterol by cells expressing SR-BI, thereby decreasing levels in foam cells and deposition at sites involved in atherogenesis.” Id. at 6-7.

According to the summary of the invention,

Transgenic animals that do not express functional SR-BI and ApoE develop severe atherosclerosis, by age four weeks in transgenic mice. Moreover, these animals exhibit progressive heart dysfunction starting by age four-six weeks, and die by age nine weeks. Pathology shows extensive fibrosis of the heart and occlusion of coronary arteries. The occlusion appears to be due to atherosclerosis, since fat deposition is in the walls. These animals are good models for the following diseases, and for screening of drugs useful in the treatment and/or prevention of these disorders:

cardiac fibrosis, myocardial infarction, defects in electrical conductance, atherosclerosis, unstable plaque, and stroke. In contrast to other known models for atherosclerosis, these animals do not have to be fed extreme diets for long periods before developing atherosclerosis and heart dysfunction. No other known model for heart attacks and stroke with these characteristics is known.

Id. at 8.

The specification teaches further that

a number of compounds are useful in altering lipid levels and cholesterol metabolism. A preferred class of compounds are PROBUCOL . . . and monoesters of PROBUCOL PROBUCOL has two known effects: (1)hypercholesteromic agent (reduces plasma cholesterol, HDL and LDL in humans – side effects, causes long QT syndrome, which their esters avoid, as well as decrease in HDL) and (2) antioxidant, may also play a role in fertility.

* * *

Based on the PROBUCOL data, other compounds that will be effective include other hypcholesteremic and antioxidant compounds, including vitamin E and vitamin C, as fertility enhancing agents as well as for treatment and/or prevention of cardiovascular disease or atherosclerosis. The preferred compounds would have both activities.

Id. at 10.

DISCUSSION

Claims 1-8 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that

the specification, while being enabling for a method for identifying compounds for treating or preventing atherosclerosis or cardiovascular disease comprising administering compounds that may have an effect on disorders selected from the group consisting of cardiac fibrosis, myocardial infarction, defects in electrical conductance, atherosclerosis, unstable plaque and stroke to a transgenic mouse whose genome comprises homozygous disruptions in the SR-BI and ApoE genes that inhibit expression of active SR-BI and Apo-E, wherein the mouse develops

atherosclerotic plaque in the aortic sinuses and progressive heart block and determining the effects of the compound on cardiac fibrosis, myocardial infarction, defects in electrical conductance, atherosclerosis, unstable plaque, stroke, diseases associated with abnormal cardiac structure or function, or elevated cholesterol or lipoprotein levels in the mouse relative to control mice not treated with the compound, does not reasonably provide enablement for the method comprising administering a compound to a mouse having decreased expression of active SR-BI and ApoE for reasons presented in the office actions mailed August 25, 2004 and March 16, 2005. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Examiner's Answer, page 3.

"[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) (emphasis in original). "[It] is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." Id. at 224, 169 USPQ at 370. Here, the examiner has not provided "acceptable evidence or reasoning which is inconsistent" with the specification, and therefore has not met the initial burden of showing nonenablement.

While the examiner engages in a Wands analysis, see In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988) (noting that facts that should be considered in determining whether a specification is enabling include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims), the examiner's primary concern appears to be that “[t]he specification, however, discloses only one mouse that exhibits this claimed combination of genotype and phenotype, that is a transgenic mouse whose genome comprises a homozygous disruption of SR-BI and ApoE.” Examiner's Answer, page 4. According to the examiner, “[t]here is no disclosure in the specification that other mice are available with decreased expression of active SR-BI and ApoE that develop atherosclerotic plaques in the aortic sinuses and progressive heart block.” Id. The examiner, however, provides no evidence that it would require an undue amount of experimentation to produce additional knockout mice and test them for the phenotype required by the claims.

The examiner notes that single knockout mice are reported in the specification, but that no analysis of the genotypes of those mice is reported. See id. at 5. The examiner thus concludes that “there is no guidance in the specification for a mouse with decreased expression of active SR-BI and Apo-E that develop atherosclerotic plaques in the aortic sinuses and progressive heart block other than the SR-BI -/- ApoE -/- mouse.” Id.

Again, the examiner has provided no evidence or scientific reasoning to support those assertions, and thus has not met his burden in demonstrating that the specification fails to enable the full scope of the claimed subject matter. In addition, a claim may encompass inoperative embodiments and still meet the enablement requirement of 35 U.S.C. § 112, first paragraph. See Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984), In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 218 (CCPA 1976), In re Cook, 439 F.2d 730, 732, 169 USPQ 298, 300 (CCPA 1971).

Therefore, as the examiner has failed to set forth a prima facie case of unpatentability under 35 U.S.C. § 112, first paragraph, we are compelled to reverse the rejection.

Claims 13, 15 and 16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Baldassarre.

According to the rejection:

Baldassarre teaches the administration of a formulation of probucol [(4,4'-(isopropylidenedithio)bis(2,6-di-t-butylphenol)], as a therapy to inhibit intimal wall thickening, a process that leads to atherosclerosis and cardiovascular disease and as a therapy to decrease total cholesterol (page 788, col. 1, parag. 1 and 2, and table 2). The reduction in intimal wall thickening and cholesterol levels is treatment or prevention of a disorder other than atherosclerosis. Baldassarre states that the criteria for entry into the clinical trial for probucol was primary hyperlipoproteinemia, which is a disease due to abnormalities in cholesterol metabolism (page 785, col. 1, parag. 2, lines 1-4). Thus, Baldassarre clearly anticipates the claimed invention.

Examiner's Answer, page 6.

In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997).

Appellants argue that “Baldasarre describes administering probucol to patients with atherosclerosis or with a genetic defect causing familial combined hyperlipidemia,” and that “[t]he first group is specifically excluded by the claims; the second is not mediated by SR-BI, but a defect in a different protein involved in hypercholesterolemia.” Appeal Brief, page 14. We agree, and the rejection is reversed.

The examiner argues that “Baldassarre teaches the administration of probucol to atherosclerosis patients to decrease serum cholesterol. SR-BI mediates an increase in serum cholesterol.” Examiner’s Answer, page 9. But as noted by appellants, the study “was for the express purpose of treating or preventing atherosclerosis,” which is specifically excluded by the claim language. Reply Brief, page 7.

Claims 13-16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Azen.

According to the rejection:

Azen teaches the oral administration of vitamin E and vitamin C to patients reduces the levels of total cholesterol and LDL cholesterol (page 2370, Table 1). Further, Azen teaches that administration of vitamin C decreases intima thickness (page 2371, column 1, paragraph 3). Azen also discloses that vitamin E reduced coronary artery lesion progression (page 2371, col. 1, parag. 2, lines 5-9). Each of reducing levels of total cholesterol,

LDL cholesterol and intima thickening are “other than atherosclerosis.”⁴, sic] Thus, Azen clearly anticipates the claimed invention.

Examiner’s Answer, page 6.

Appellants argue that the patients who were treated by Azen all had atherosclerosis, and that was in fact a criteria of the study. Appeal Brief, page 16. We agree, and the rejection is reversed.

OTHER ISSUES

We point the examiner’s attention to the following art, which may have a bearing on the patentability of claims 13-16.

BellaOnline^{SM4} discusses the use of vitamin supplements in the treatment of fertility, a disease other than atherosclerosis, mentioned in the specification and discussed by counsel at the oral hearing as a disease other than atherosclerosis, that could be treated by the method of claims 13-16. Although copyrighted in 2006, the webpage references an article by Bayer,⁵ published in 1960, that states that in a preliminary human trial, infertile couples given vitamin E showed a significant increase in fertility.

Miettinen⁶ discusses the use of probucol in prevention of cardiovascular diseases, and states that the incidence of stroke, a disease other than atherosclerosis discussed in the specification and the claims as originally filed, is decreased in the group that received probucol.

⁴ BellaOnline, <http://www.bellaonline.com/articles/art32665.asp>, printed out September 5, 2006.

⁵ Bayer, R., “Treatment of infertility with vitamin E,” Int. J. Fertil., Vol. 5, pp. 70-8 (1960).

CONCLUSION

Because the examiner has failed to set forth a prima facie case of unpatentability, we reverse the rejections under 35 U.S.C. § 112, first paragraph, and under 35 U.S.C. § 102(b). Because appellants do not contest the obviousness-type double patenting rejection, that rejection is summarily affirmed. Finally, we have raised other issues that the examiner may wish to address upon return of the application.

AFFIRMED-IN-PART; REVERSED-IN-PART

Donald E. Adams)
Administrative Patent Judge)
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) BOARD OF PATENT
Demetra J. Mills)
Administrative Patent Judge) APPEALS AND
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) INTERFERENCES
)
Lora M. Green)
Administrative Patent Judge)

⁶ Miettinen et al. (Miettinen), "Multifactorial primary prevention of cardiovascular diseases in middle-aged men. Risk factor changes, incidence, and mortality," Journal of the American Medical Association, Vol. 254, No. 15, 1985 (abstract only).

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