

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 45

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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

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Ex parte MICHAEL R. HAYDEN,  
YUANHONG MA,  
SUZANNE LEWIS, and  
GUOQUING LIU

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Appeal No. 2003-1170  
Application No. 08/817,192

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HEARD: January 6, 2004

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Before WILLIAM F. SMITH, GRIMES, and GREEN, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 50 through 57, all the claims pending in the application. Claim 50 is representative of the subject matter on appeal and reads as follows:

50. A method for preventing or delaying the onset of coronary artery disease in a human individual having lipoprotein lipase enzyme in which a serine residue is present at amino acid 291 in the enzyme, comprising administering to the individual a polynucleotide encoding a replacement lipoprotein lipase enzyme, said replacement lipoprotein lipase enzyme having an asparagine residue as amino acid 291 in the replacement enzyme, wherein the replacement lipoprotein lipase gene is expressed in the individual to produce a functional lipoprotein lipase enzyme.

The references relied upon by the examiner are:

Galton et al. (Galton), "Polymorphisms of the Lipoprotein Lipase Gene and Premature Atherosclerosis," Journal of Internal Medicine, Vol. 236, Suppl. 736, pp. 63-68 (1994)

Orkin et al. (Orkin), Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy, issued by the U.S. National Institutes of Health on December 7, 1995

Verma et al. (Verma), "Gene Therapy-Promises, Problems and Prospects," Nature, Vol. 389, pp. 239-242 (Sept. 1997)

Claims 50 through 57 stand rejected under 35 U.S.C. § 112, first paragraph (enablement). We reverse.

#### Background

The present invention involves the human lipoprotein lipase gene. As explained by appellants:

It has now been found that a single point mutation in the human lipoprotein lipase gene which results in an A - G nucleotide change at codon 291 (nucleotide 1127) of the lipoprotein lipase gene, and a substitution of serine for the normal asparagine in the lipoprotein lipase gene product is seen with increased frequency in patients with coronary artery disease, and is associated with an increased susceptibility to coronary artery disease, including in particular premature atherosclerosis. This is expressed as a diminished catalytic activity of lipoprotein lipase, lower HDL-cholesterol levels and higher triglyceride levels.

Specification, page 2, lines 16-22.

The claimed invention under review in this appeal involves a method of gene therapy in which a defined replacement lipoprotein lipase gene is expressed in an individual in which the lipoprotein lipase enzyme has a serine residue present at amino acid 291 to produce a more fully functional lipoprotein lipase enzyme.

#### Discussion

There are two main aspects to the examiner's enablement rejection. First, the examiner considers gene therapy in and of itself to be a highly unpredictable art. See, e.g., Examiner's Answer, page 5 ("Gene therapy has been and remains a highly unpredictable and undeveloped art."). The second aspect involves the claim language which states that the claimed method is for "preventing or delaying the onset of coronary artery disease." The examiner observes that coronary artery disease can be attributed to a wide variety of causes or contributing factors and that "it is highly unlikely that a defect in lipoprotein lipase function would be the sole causative factor in the human individuals carrying such a defect." Examiner's Answer, pages 6-7.

Turning to the first aspect of the examiner's rejection, we find that the examiner's focus on gene therapy in general is misplaced. It appears that the examiner believes that in order for the claimed invention to be enabled that one of skill in the art must be convinced that the claimed method will result in a therapeutic effect. The examiner explains:

Orkin and Galton were provided as evidence that the specific therapy claimed would be unlikely to achieve the therapeutic effect required by the preamble, that coronary artery disease be either prevented or its onset be delayed. Even normal individuals may develop coronary artery disease from a variety of environmental factors or genetic factors other than LPL deficiency. Orkin and Verma show that it is unlikely that the claimed methods would be able to restore the lipoprotein lipase of the recited individual to normal levels, particularly since prior experience with gene therapy protocols indicated that achieving insufficient expression and lack of persistent expression from the vector were significant problems, and thus far unattained. At best, the claimed therapy would only result in reducing the severity of the deficiency, and the treated individual would still be prone to the same contributing factors as normal individuals.

Examiner's Answer, page 9, first full paragraph.

We note that lack of conclusive evidence that a claimed invention provides therapeutic or human efficacy does not necessarily mean that the claimed invention is not enabled. As explained by our appellate reviewing court, “[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans.” In re Brana, 51 F.3d 1560, 1568, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995). In Brana, the court observed that an invention need not have entered Phase II clinical trials in order to be considered useful under the patent laws. Id., at 1568, 34 USPQ2d at 1442-1443. In other words, a claimed invention may be considered useful or enabled under the patent statutes at a time before the claimed invention is conclusively shown to have a clinical or therapeutic effect.

Here, the examiner relies upon Orkin, Verma, and Galton to support his view that the field of gene therapy in general is unpredictable. In our view these references do not establish that the field of gene therapy is as unpredictable as the examiner believes. For example, Verma states:

Although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story. To explore why this is the case, we will use our own experience and other examples to look at the many technical, logistical and, in some cases, conceptual hurdles that need to be overcome before gene therapy becomes routine practice in medicine.

As seen from Verma, gene therapy is not a “routine practice in medicine” even though many clinical trials involving gene therapy have been conducted. However, a claimed method need not be a “routine practice in medicine” in order for it to be

considered enabled under the patent statutes since the legal requirements of enablement envision that further experimentation and refinement of the claimed invention may be necessary before it reaches that stage. In re Brana, supra.

Absent a fact-based explanation from the examiner based upon the correct legal standard, i.e., one that does not require gene therapy being a “routine practice of medicine,” we do not find that the examiner has established a prima facie case of nonenablement.

The second aspect of the examiner’s rejection is based upon an unreasonable reading of the claims. Claim 50 is directed to a method for preventing or delaying the onset of coronary artery disease in a human individual having lipoprotein lipase enzyme in which a serine residue is present at amino acid 291 in the enzyme. Focusing on that individual patient, it seems reasonable that administering the claimed polynucleotide to produce a functional lipoprotein lipase enzyme in the individual would reasonably be expected to prevent or delay the onset of coronary artery disease in that individual to the extent that individual is at an increased risk of coronary artery disease due to the presence of the defective gene. We think it is an unreasonable reading of the claims to require that the result of the claim be that the treated individual be, in effect, guaranteed to be forever free of coronary artery disease. That reading of the claim is unrealistic. Treating one factor of a multifactorial condition, as set forth in claim 50, would reasonably be expected to delay or prevent the onset of the condition.

The examiner’s decision is reversed.

REVERSED

William F. Smith )  
Administrative Patent Judge )  
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) BOARD OF PATENT  
Eric Grimes )  
Administrative Patent Judge ) APPEALS AND  
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) INTERFERENCES  
Lora M. Green )  
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