

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

Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte KEITH D. LINDOR

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Appeal No. 1998-2267  
Application 08/339,084

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HEARD: April 24, 2001

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Before ROBINSON, 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 1-8, which are all of the claims pending in this application.

We reverse.

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

1. A therapeutic method for the treatment of nonalcoholic steatohepatitis comprising administering to a human patient in need of such treatment an effective amount

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of ursodeoxycholic acid, a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable ester thereof.

The prior art references relied upon by the examiner are:

Shironaga<sup>1</sup>                                      JP 61-158995 KOKAI                                      July 18, 1986

Podda et al. (Podda), "Effect of Different Doses of Ursodeoxycholic Acid in Chronic Liver Disease", Digestive Diseases and Sciences, Vol. 34., No. 12, pp. 59S-69S (1989)

Reference relied on by appellant:

(Kaplowitz), Biliary Diseases, pp. 327-337, 383, 445-446 and index, (Neil Kaplowitz ed., Wilkins and Wilkins 1992)

#### Ground of Rejection

Claims 1-8 stand rejected under 35 U.S.C. § 103 over Podda in view of Shironaga.

### DISCUSSION

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

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellant regarding the noted rejection, we make reference to the examiner's Answer for

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<sup>1</sup> The examiner relied on an abstract of the Japanese patent application from HCAPLUS (Abstract 224). Appellant provided an English translation of the entire Japanese patent application with the Brief (Appendix IV), which we rely on for purposes of this appeal.

the examiner's reasoning in support of the rejection, and to the appellant's Brief for the appellant's arguments thereagainst. As a consequence of our review, we make the determinations which follow.

35 U.S.C. § 103

Claims 1-8 stand rejected under 35 U.S.C. § 103 over Podda in view of Shironaga.

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.

Nonalcoholic steatohepatitis (NASH) is a liver condition which involves the development of histologic changes in the liver which are comparable to those induced by excessive alcohol intake, but in the absence of alcohol. NASH is commonly associated with hyperlipidemia, obesity, and type II diabetes mellitus. Specification, page 1.

In the present case, the examiner relies on Podda for establishing that ursodeoxycholic acid (UDCA) is known to be useful in the treatment of chronic liver disease. Answer, page 4. The examiner acknowledges that Podda does not disclose the use of UDCA for the treatment of NASH.<sup>2</sup>

Shironaga is relied on for the disclosure of the use of UDCA for the treatment of fatty liver. Shironaga describes the inducement of a fatty liver condition in SRF mice using a “stone-inducing diet”, which is a normal diet containing 1% cholesterol and 0.5% cholic acid. An increase in liver weight was confirmed by histological and biochemical testing. Shironaga, English translation, page 6.

The examiner summarizes (Answer, page 5) that:

One of ordinary skill in the art would have been motivated to employ UDCA in the treatment of NASH, a well known type of hepatitis characterized by fat abnormalities in the hepatic tissue, since UDCA was known for the treatment of various chronic liver diseases, and known for the treatment of another disease involving fat abnormalities in the hepatic tissue.

Where the prior art, as here, gives reason or motivation to make the claimed invention, the burden then falls on an appellant 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)

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<sup>2</sup> Appellant, however, does admit that NASH is considered a chronic liver disorder. Lindor Declaration of February 19, 1996, pages 2-3.

(en banc), cert. denied, 500 U.S. 904 (1991). Accordingly, we carefully evaluate the objective evidence of nonobviousness supplied by the appellant.

Appellant submits two declarations of Dr. Keith Lindor as evidence of the non-obviousness of the claimed invention. The Declaration of Lindor dated February 19, 1996, suggests that Podda describes three distinct liver pathologies, primary biliary cirrhosis, primary sclerosing cholangitis and chronic hepatitis which are unrelated to NASH. Declaration, paragraphs 4-7. Dr. Lindor suggests that “fatty liver” as described in Shironaga, can be caused by many organic diseases and external toxins and that there would be no reason for one of skill in the art, in possession of Shironaga “to conclude that the administration of UDCA to humans with NASH would be an efficacious treatment.” Declaration, paragraph 9.

The second Declaration of Dr. Lindor, dated February 23, 1996, provides evidence, Kaplowitz, indicating that “NASH differs from fatty liver in that parenchymal inflammatory changes and the presence of Mallory's hyalin are noted. Additionally, NASH may progress to fibrosis or cirrhosis in one-third of cases, an outcome not usually associated with fatty liver.” Kaplowitz, page 445. The second Declaration of Lindor states that “those of skill in the art do not consider NASH under the rubric of chronic hepatitis, nor do those of skill in the art consider the two diseases to be equivalents.” Declaration, page 2. Further, the second Lindor Declaration suggests that Shironaga does not establish a mouse model

which can be correlated to any human liver disease, much less the treatment of NASH.

Declaration, page 3. In sum, appellant argues the examiner has failed to show that one of ordinary skill in the art would consider the conditions of Podda and Shironaga to be equivalents of NASH. Brief, pages 11-12.

In response to appellant's arguments and evidence, the examiner indicates that the rejection of the claims "is not based on any asserted 'equivalency' between the liver disorders discussed herein, but instead on certain significant known similarities between these disorders and NASH which would have provided ample motivation or suggestion to one of ordinary skill in the art to arrive at the claimed invention." Answer, page 10.

A conclusion of prima facie obviousness, of course, does not end a patentability determination under 35 U.S.C. § 103. As stated in In re Hedges, 783 F.2d 1038, 1039, 228 USPQ 685, 686 (Fed. Cir. 1986):

If a prima facie case is made in the first instance, and if the applicant comes forward with reasonable rebuttal, whether buttressed by experiment, prior art references, or argument, the entire merits of the matter are to be reweighed. In re Piasecki, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984).

We find that the examiner errs in only taking into account the similarities of the reference and claimed liver conditions, and in failing to reevaluate the evidence and to account for the differences between the liver conditions described by Podda and Shironaga and the NASH condition. In particular, the examiner has failed to rebut

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statements and evidence, Kaplowitz, cited by appellant which would reasonably appear to establish that NASH is distinct from the fatty liver condition described by Shironaga and the conditions described by Podda.

After evidence or arguments are submitted by the appellant 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. On balance, we believe that the totality of the evidence presented by the examiner and appellant weighs in favor of finding the claimed invention to be non-obvious in view of the cited references. We find the examiner has not established on the record before us that the cited references both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art. The rejection of the claims for obviousness of the claimed invention is reversed.

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CONCLUSION

The rejection of claims 1-8 under 35 U.S.C. § 103 is reversed.

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

REVERSED

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Douglas W. Robinson	)	
Administrative Patent Judge	)	
	)	
	)	
	)	BOARD OF PATENT
Demetra J. Mills	)	
Administrative Patent Judge	)	APPEALS AND
	)	
	)	INTERFERENCES
	)	
Eric Grimes	)	
Administrative Patent Judge	)	

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