

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 28

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte CESARE SIRTORI,
GUIDO FRANCESCHINI,
LARS ABRAHMSEN,
MATS LAKE, LIDINGO,
JOANNA CHMIELEWSKA, and
PETER LIND

Appeal No. 2002-1547
Application No. 09/259,434

ON BRIEF

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

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

Appellants have requested an oral hearing in this case, but on reviewing the case, we have determined that an oral hearing is not necessary. We render the following decision based on the written record. See 37 CFR § 1.194(c).

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-5, 8, 9, 11-16, and 18. Claims 17, 19, 20, and 22 are

appears that these subjects may be “protected” from atherosclerosis.

Another very specific feature of the Apo AI-M, is its capacity to form dimers with itself and complexes with Apo AII, in both cases because of the presence of the Cys residue. From studies of blood fractions containing a mixture of Apolipoproteins, there were indications, showing that the presence of dimers and complexes in the circulation may be responsible for the increased elimination half-life of these in the carriers, recently described in clinical studies.

Id., pages 4-5.

The specification discloses recombinant production of Apo AI-M dimers. (pages 14-21) and purification of the Apo AI-M dimers from the plasma of subjects carrying the Apo AI-M mutation. See pages 10-13. The dimers were purified directly from plasma by two steps of chromatography on a “Sephacryl S-300 HR column (2.6 x 300 cm).” Page 10. The resulting dimer preparations are disclosed to be “>98% pure.” Id.

The specification also discloses that Apo AI-M dimers can be made by isolating Apo AI-M monomers, then converting them to dimers. See pages 10-13. Monomers were purified by a single step of chromatography on a “Sephacryl S-200 column (2.6 x 150 cm),” followed by chromatography on a “Thiopropyl-Sepharose column” to separate normal Apo AI from Apo AI-M. See pages 10-11. The Apo AI-M monomers were then converted to dimers by oxidation, resulting in up to 36.1% dimer formation. See pages 12-13.

The plasma-purified dimers were characterized by several methods. Circular dichroism spectroscopy showed that the purified dimers had an α -helix

content of 52.2% at a concentration of 0.1 mg/ml and 57.8% at 1.1 mg/ml. See page 22.

Discussion

Claim 1 is representative of the claimed invention, and is directed to a composition comprising isolated Apolipoprotein AI-Milano dimers purified to at least 90% homogeneity.

The examiner rejected the claims as obvious in view of Sirtori. The examiner characterized Sirtori as

teach[ing] that Apolipoprotein A1-Milano has the capacity to naturally form dimers with itself . . . and the Apolipoprotein A1-Milano dimers have a prolonged half-life, and thus remain in the circulation for longer periods and exert their arterial protective activity better than normal Apolipoprotein A1. . . . Sirtori et al. expressed Apolipoprotein A1-Milano in yeast and characterized its structure.

Examiner's Answer, page 3. She concluded that

[i]t would have been obvious to a person of ordinary skill in the art to make purified Apolipoprotein A1-Milano dimers because Sirtori et al. teach that these dimers naturally form and, though Sirtori et al. do not show that the Apolipoprotein A1-Milano used in their experiments were dimers, dimers of Apolipoprotein A1-Milano naturally occur and have arterial protective activity. . . . [I]t would have been obvious to a person of ordinary skill in the art to treat cardiovascular diseases associated with thrombosis with active dimers of Apolipoprotein A1-Milano because one would expect that these dimers would have been part of the composition of Sirtori et al.

Id., pages 4-5.

Appellants argue that

Sirtori does not make obvious a method for achieving dimer concentrations that are at least 90% pure. The purification scheme disclosed by Sirtori teaches away from the purification of Apo-A1-M

dimers purified to greater than 90% purity. . . . Relying on Sirtori's method for Apo-A1-M purification, a person of ordinary skill in the art would fail to purify dimers of Apo-A1-M away from monomers of Apo-A1-M because the method cannot produce Apo-A1-M purified to greater than 90%. Thus, Sirtori, taken as a whole, does not provide the motivation or the means to purify the Apo-A1-M dimer preparations of greater than 90% purity.

Appeal Brief, pages 8-9. The examiner acknowledged Appellants' argument on this point, and responded that "[t]he rejection acknowledges these failings."

Examiner's Answer, page 6.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). The prima facie case must account for all the limitations of the claims. See General Foods Corp. v. Studiengesellschaft Kohle mbH, 972 F.2d 1272, 1275, 23 USPQ2d 1839, 1840 (Fed. Cir. 1992) ("[E]ach claim is an entity which must be considered as a whole," emphasis in original); In re Angstadt, 537 F.2d 498, 501, 190 USPQ 214, 217 (CCPA 1976) ("[W]e must give effect to all claim limitations," emphasis in original).

We agree with Appellants that Sirtori does not support a prima facie case under 35 U.S.C. § 103. The claims on appeal are limited to compositions comprising Apo AI-M dimers "purified to at least 90% homogeneity." The specification discloses that the claimed composition can be isolated from plasma by two steps of chromatography on a "Sephacryl S-300 HR column (2.6 x 300 cm)." Page 10. By contrast, Apo AI-M monomers were purified by

chromatography on a “Sephacryl S-200 column (2.6 x 150 cm),” followed by chromatography on a “Thiopropyl-Sepharose column.” See pages 10-11. When the monomers were dimerized, the resulting compositions comprised no more than 36.1% dimers. See pages 12-13.

Sirtori discloses purification of recombinant Apo AI-M by chromatography on either a “Sephacryl S-200 column and/or an anti-apo AI-Sepharose column.” Page 12. The examiner has pointed to no other disclosure in Sirtori that would teach or suggest other purification methods to those skilled in the art. Nor has the examiner presented evidence that either of the disclosed methods would purify Apo AI-M dimers to at least 90% homogeneity. The evidence, in fact, is to the contrary. The instant specification discloses that Sephacryl S-200 chromatography does not result in a purified dimer preparation, but rather produces monomers that must be oxidized to produce even a reasonable (36%) amount of dimers.

In addition, Sirtori analyzed the purified Apo AI-M by circular dichroism (CD) spectroscopy and found that it had an α -helix content of 43%, lower than the 52% found for normal Apo AI. See page 12. The instant specification, on the other hand, discloses that purified Apo AI-M dimers have an α -helix content of 52.2% to 57.8%, depending on protein concentration. See page 22. The CD spectroscopy data provide further evidence that Apo AI-M composition disclosed by Sirtori does not contain Apo AI-M dimers purified to at least 90% homogeneity.

It is true that Sirtori disclosed that the Apo AI-Milano mutant could form dimers, and that the dimers were probably responsible for the longer half-life of Apo AI-Milano in circulation compared to normal Apo AI. See pages 4-5. Thus, Sirtori may have motivated a person of ordinary skill in the art to try to make dimers. However, in the absence of adequate direction regarding how to do so, Sirtori at best makes the composition of the instant claims “obvious to try.” See In re Eli Lilly & Co., 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990) (“An ‘obvious-to-try’ situation exists when a general disclosure may pique the scientist’s curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result.”).

Other Issue

Appellants’ previous application 08/104,063 issued as U.S. Patent 5,876,968 and contains claims that are very similar to some of the claims in the instant application. Appellants have filed a terminal disclaimer in this case, obviating any obviousness-type double patenting issue. See Paper No. 4, filed September 13, 1999. We note, however, that instant claim 19 appears to be directed to the same invention as that of patented claim 3, and that a terminal disclaimer does not obviate a rejection for “same invention” double patenting.

Upon return of this case, the examiner should review the pending claims and ensure that none of the claims are directed to the same invention as the claims in Appellants’ ‘968 patent. If the instant claims are directed to the same

invention as those of the patent, a rejection under 35 U.S.C. § 101 for double patenting would be appropriate.

Summary

The cited reference does not teach or suggest any method for making the claimed composition, comprising Apo AI-M dimers “purified to at least 90% homogeneity.” Therefore, the reference supports at best an “obvious to try” rationale, which is insufficient to show obviousness under 35 U.S.C. § 103. The examiner’s rejection is reversed.

REVERSED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
ERIC GRIMES)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
)	
LORA M. GREEN)	
Administrative Patent Judge)	

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PATREA L PABST
ARNALL GOLDEN & GREGORY
2800 ONE ATLANTIC CENTER
1201 WEST PEACHTREE STREET
ATLANTA, GA 30309-3450

EG/jlb