

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. 30

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ANDREW S. JANOFF, MIRCEA C. POPESCU,
ALAN L. WEINER, LOIS E. BOLCSAK,
PAUL A. TREMBLAY, and CHRISTINE E. SWENSON

Appeal No. 98-2247
Application No. 08/108,822

HEARD
MAY 10, 2001

Before KIMLIN, PAK and LIEBERMAN, Administrative Patent Judges.

LIEBERMAN, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the decision of the examiner refusing to allow claims 129, 131 and 136 through 151, which are all of the claims pending in this application.

THE INVENTION

The invention is directed to a method of preparing a pharmaceutical composition wherein a salt form of an organic acid sterol derivative in an amount sufficient to form a closed vesicle is mixed with an aqueous phase and agitated until the vesicles are formed. The mixture is essentially free of organic solvent. Other features of the claimed subject matter are set forth in the following illustrative claim.

THE CLAIMS

Claims 129 is illustrative of appellants' invention and is reproduced below.

129. A method for preparing a pharmaceutical composition which comprises liposomes having bilayers comprising a lipid which consists essentially of a salt form of an organic acid sterol derivative capable of forming closed bilayers, the method comprising:

(i) mixing an amount of the salt form of the organic acid sterol derivative sufficient to form closed vesicles with an aqueous phase so as to form a mixture comprising the aqueous phase and the sterol derivative, wherein the mixture is essentially free of organic solvent; and

(ii) agitating the mixture until vesicles are formed,
wherein when the sterol derivative is negatively charged at neutral pH the mixture is substantially free of multivalent cations or when the derivative is positively charged at neutral pH the mixture is substantially free of multivalent anions.

THE REFERENCES OF RECORD

As evidence of obviousness, the examiner relies upon the following references.

Panzarella	3,197,367	July 27, 1965
Klein	3,859,047	Jan. 7, 1975

James E. F. Reynolds (ed.), Martindale The Extra Pharmacopoeia, pp. 726-727 (28th ed., The Pharmaceutical Press, London, 1982).

Marc J. Ostro (ed.), Liposomes, pp. 29-39 (Marcel Dekker, Inc., New York, 1983).

THE REJECTIONS

Claims 129, 131, 137 through 145 and 150 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ostro in view of Klein.

Claim 136 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Ostro in view of Klein and further in view of Martindale.

Claims 147, 149 and 151 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ostro in view of Klein and further in view of Panzarella.

Claims 120 [sic., 129], and 137 through 151 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which appellants regard as the invention.¹

¹On the record before us it is clear that the statement of the rejection is directed to claim 129 not claim 120. Claim 120 was canceled in the amendment dated September 25, 1995. In addition reference to the

OPINION

We have carefully considered all of the arguments advanced by the appellants and the examiner and agree with the appellants that the rejections of claims 129, 131 and 136 through 151, are not well founded. Accordingly, we reverse each of the rejections.

The Rejection under 35 U.S.C. §112, Second Paragraph

“The legal standard for definiteness under the second paragraph of 35 U.S.C. § 112 is whether a claim reasonably apprises those of ordinary skill in the art of its scope.” *In re Warmerdam*, 33 F.3d 1354, 1361, 31 USPQ2d 1754, 1759 (Fed. Cir. 1994). The inquiry is to determine whether the claim sets out and circumscribes a particular area with a reasonable degree of precision and particularity. The definiteness of the language employed in a claim must be analyzed not in a vacuum, but in light of the teachings of the particular application. *In re Moore*, 439 F.2d 1232, 1235, 169 USPO 236, 238 (CCPA 1971).

It is the examiner’s position that the claimed subject matter is indefinite in “not reciting that the aqueous phase contains a bioactive agent in the event that the salt-forming base is not itself a bioactive agent.” See Answer, page 8. In our view, the examiner’s submission is directed to the broadness of the claimed subject matter as

Answer, pages 3 and 8 in conjunction with the appellants supporting statement at Oral Hearing necessarily leads us to conclude that the independent claim at issue in the rejection under the second paragraph of 35 U.S.C. § 112 is claim 129, not claim 120.

opposed to the definiteness of the claimed subject matter.

However, it is well settled that breadth does not necessarily render a claim indefinite and the examiner has stated no other ground of rejection. *In re Gardner*, 427 F.2d 786, 788, 166 USPO 138, 140 (CCPA 1970) (“Breadth is not indefiniteness.”); *In re Borkowski*, 422 F.2d 904, 909, 164 USPO 642, 645-46 (CCPA 1970).

Furthermore, we find that the description in the specification, page 17, provides for the addition of a water soluble compound to previously formed liposomes in at least one disclosed embodiment. Therefore, liposomes may be prepared in the absence of a water soluble compound, such as a bioactive agent, which agent is not a necessary element as alleged on the record before us. Accordingly, the claimed subject matter directed to the formation of a liposome in the absence of a water soluble compound, such as a bioactive agent, is not indefinite

On this record, we conclude that the specification provides a reasonable standard for understanding the metes and bounds of the claimed subject matter, when the claims are read in light of the specification. *Seattle Box Co. v. Industrial Crating & Packing, Inc.*, 731 F.2d 818, 826, 221 USPO 568, 573-574 (Fed. Cir. 1983). Accordingly, we reverse the rejection of the examiner.

The Rejection under 35 U.S.C. § 103

“ [T]he examiner bears the initial burden, on review of the prior art or on any

other ground, of presenting a *prima facie* case of unpatentability," whether on the grounds of anticipation or obviousness. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On the record before us, the examiner relies upon four separate rejections to establish a *prima facie* case of obviousness. Each of the four rejections however, are directed to a single premise. It is the position of the examiner that, "it would have been obvious at the time the applicants' invention was made to use one of the stated salts shown to be old by Klein (abstract; Ex's 1 - 4) in lieu of, or in addition to, the phospholipids in the methods of Ostro to produce steroidal liposomes." See Answer, pages 5 and 6. We disagree.

The examiner has relied upon Ostro as the primary reference in each of the rejections under Section 103. Ostro discloses a plurality of methods for the preparation of liposomes.² See pages 33 to 39. The methods include preparing the liposomes either in the presence of organic solvent or in the absence of organic solvent. We find that the preparation of small unilamellar vesicles occurs in the absence of organic solvent. See page 33. Similarly, we find that multilamellar vesicles are prepared in the absence of organic solvent. See page 36 and 37. Alternately organic solvent may be present during the formation of vesicles. See pages 38 and 39.

Ostro however, is silent as to which lipids may be used to form liposome vesicles.

² A liposome is defined as an artificial vesicle composed of one or more concentric phospholipid bilayers. See Webster's Ninth New Collegiate Dictionary, page 696, Merriam-Webster Inc. Springfield, MA 1986.

The sole relevant statement in this respect found in Ostro is that, "[t]he lipid is not necessarily phospholipid but this is the most commonly used component." See page 28. The examiner however, apparently interprets the statement in Ostro as providing for the utilization of any lipid in liposome formation. Accordingly, the examiner concludes that the disclosure of appellants' preferred lipid by Klein is sufficient to establish a *prima facie* case of obviousness.

In reaching that conclusion, however, the record before us is necessarily based upon several unsupported assumptions. Initially, it is requisite that lipids in general are able to form liposomes. On this record, that fact has not been established. It is further assumed on the record that the cholesteryl hemisuccinate disclosed by Klein is a lipid. Klein however, never states that cholesteryl hemisuccinate is a lipid.

Moreover, lipids have been defined in part as "[a]ny of a group of substances that generally are soluble in ether, chloroform or other solvents for fats, but are only sparingly soluble in water."³ In contrast, although Klein discloses a preferred sterol salt of the claimed subject matter, cholesteryl hemisuccinate, we find that Klein describes cholesteryl hemisuccinate as a water soluble cholesterol salt. See Abstract, column 2, lines 6-8, 42-52, and 68 through column 3, line 1. Accordingly, on this record, the examiner fails to establish as a fact that the cholesteryl hemisuccinate is a lipid.

³See *Webster's Third New International Dictionary*, p. 1318 G. & C. Merriam Co., 1971.

It is well settled that it is the examiner who has the burden of establishing that one of ordinary skill in the art would have found the requisite motivation and reasonable expectation of success for the proposed modification from the applied prior art teachings. See *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). It is reasonable to conclude based upon the above findings that there is neither a suggestion in the art of record to utilize the cholesteryl hemisuccinate of Klein to form a liposome, nor a reasonable expectation of success was fully employing cholesterol derivative of Klein in liposome formation.

Finally, the references to both Martindale and Panzarella are directed to limitations present in dependent claims, but do not remedy the deficiencies discussed above.

Accordingly, the rejections of the examiner are reversed.

Decision

The rejection of claims 129, 131, 137 through 145 and 150 under 35 U.S.C. § 103(a) as being unpatentable over Ostro in view of Klein is reversed.

The rejection of claims 136 under 35 U.S.C. § 103(a) as being unpatentable over Ostro in view of Klein and further in view of Martindale is reversed.

The rejection of claims 147, 149 and 151 under 35 U.S.C. § 103(a) as being unpatentable over Ostro in view of Klein and further in view of Panzarella is reversed.

The rejection of claims 120 [sic] [129], and 137 through 151 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which appellants regard as the invention is reversed.

The decision of the examiner is reversed.

REVERSED

EDWARD C. KIMLIN
Administrative Patent Judge

CHUNG K. PAK
Administrative Patent Judge

PAUL LIEBERMAN
Administrative Patent Judge
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ROSANNE GOODMAN
THE LIPOSOME COMPANY, INC.
ONE RESEARCH WAY
PRINCETON FORRESTAL CENTER
PRINCETON , NJ 08540