The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 32

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOCELYN E. MC OSKER

Appeal No. 1996-3016
Application 08/008,859

ON BRIEF

Before WILLIAM F. SMITH, ROBINSON, and SCHEINER, 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 1 through 22, all the claims remaining in the application. Subsequent to the final rejection, claims 9, 11, 12, 14, and 15 were canceled, leaving claims 1 through 8, 10, 13, and 16 through 22 for our consideration.

Claims 1, 16, 19, and 20 are representative of the subject matter claimed and read as follows:

1. A method of treatment for osteoporosis in a human or other animal subject, comprising: administering a bone-active phosphonate to said subject, at a level of at

least about 0.1 LED per day of said treatment; and and [sic] administering an estrogen hormone to said subject, at a level of from about 0.2 to about 0.8 LED per day of said treatment.

16. A unit dosage form composition, for the treatment of osteoporosis, comprising:

(a) at least about 0.1 LED of a bone-active phosphate;

(b) from about 0.2 to about 0.8 LED of an estrogen hormone; and

(c) a pharmaceutically-acceptable carrier.

19. A unit dosage form composition, according to Claim 16, wherein said bone-active phosphonate is 2-(3-pyridyl)-1-hydroxyethane-1,1-bisphosphonic acid, or a pharmaceutically-acceptable salt or ester thereof.

20. A unit dosage form composition according to Claim 19, wherein said estrogen hormone is estradiol.

The references relied upon by the examiner are:

Francis et al. (Francis), "Chemical, Biochemical, and Medicinal Properties of the Diphosphonates," The Role of Phosphonates in Living Systems, Chapter 4, pp. 55-96 (1983)

Chesnut III, "Synthetic salmon calcitonin, diphosphonates, and anabolic steroids in the treatment of postmenopausal osteoporosis," Osteoporosis 2, Copenhagen International Symposium on Osteoporosis, pp. 549-55 (June 3-8,1984)

Lindsay et al. (Lindsay 1984), "The Minimum Effective Dose of Estrogen for Prevention of Postmenopausal Bone Loss," Journal of the American College of Obstetricians and Gynecologists, Vol. 63, No. 6, pp. 759-63 (1984)

Lindsay et al. (Lindsay 1985), "Osteoporosis Current Concepts," Bulletin of The New York Academy of Medicine, Vol. 61, No. 4, pp. 307-22 (May 1985)

Wronski et al. (Wronski), "Endocrine and Pharmacological Suppressors of Bone Turnover Protect against Osteopenia in Ovariectomized Rats," Endocrinology, Vol. 125, No. 2, pp. 810-16 (1989)

A reference of record discussed by this merits panel is:

Ettinger et al. (Ettinger), Postmenopausal Bone Loss Is Prevented by Treatment with Low-Dosage Estrogen with Calcium," Annals of Internal Medicine, Vol. 106, pp. 40-45 (1987)

Claims 1 through 8, 10, 13, and 16 through 22 stand rejected under 35 U.S.C. § 112, first paragraph (enablement). Claims 1 through 8, 10, 13, and 16 through 22 also stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies upon "Applicant's admissions," Francis, Lindsay 1984, Lindsay 1985, Wronski and Chesnut. We reverse all rejections.

DISCUSSION

We initially note that the subject matter on appeal has only been examined to the extent the claims are directed to estradiol and 2-(3-pyridyl)-1-hydroxyethane-1, 1-bisphosphonic acid in view of the election of species requirement.

1. Enablement

As stated at page 3 of the Answer, the examiner has concluded that "the disclosure is enabling only for claims limited [to] the amounts of each active agent in the alleged synergistic composition and use thereof which yields the surprising and unexpected synergistic result." The examiner's requirement appears to be a result of appellant's effort to rebut the examiner's rejection under 35 U.S.C. § 103 by way of a declaration under 37 CFR § 1.132 of appellant Jocelyn E. McOsker in which appellant characterizes the presented data as "synergistic."

Suffice it to say that the examiner has cited no legal authority for the proposition that claims pending in a patent application must be limited to the subject matter which "yields the surprising and unexpected synergistic result." Nor do we know of any legal authority which requires the claims to be so limited. Absent a fact-based explanation from the examiner as to why one skilled in the art would not be able to practice the claimed invention throughout its scope without undue experimentation, we do not find the examiner has sustained his initial burden of establishing a prima facie case of lack of enablement. The rejection under 35 U.S.C. § 112, first paragraph (enablement) is reversed.

2. Obviousness

As a result of the election of species requirement, the subject matter under review in this appeal involves the combined use of 2-(3-pyridyl)-1-hydroxyethane-1,1-bisphosphonic acid as a bone-active phosphonate and estradiol as an estrogen hormone for the purpose of treating osteoporosis. The so-called admissions relied upon by the examiner are merely appellant's description of phosphonates and estrogens which are described in the prior art as being useful individually to treat osteoporosis. That much is not disputed by applicant. What is disputed by applicant is whether the applied prior art reasonably suggests the use of an estrogen hormone for the treatment of osteoporosis in the claimed amount of "from about 0.2 to about 0.8 LED." The acronym "LED" stands for "least effective dose." As set forth at page 18, lines 8-17 of the specification, the least effective

dose is "the minimum dose of active which is effective, by itself, to cause a significant inhibition of bone resorption." The specification indicates at page 20, lines 9-22:

> Similarly, the LED of the estrogen hormone is that level of the hormone which, by itself, is effective to prevent bone loss in subjects having osteoporosis. That level is generally recognized to be about 0.625 mg per day of conjugated estrogen or an equivalent dose of other estrogen hormones (for example, 25 µg per day of ethinyl estradiol; or 2 mg per day of 17-ß-estradiol). See, Barzel, "Estrogens in the Prevention and Treatment of Post-Menopausal Osteoporosis: a Review", 85 American Journal of Medicine 847 (1988); Lindsay, et al., "The Minimum Effective Dose of Estrogen for Prevention of Post-Menopausal Bone Loss", 63 Obstetrics and Gynecology 759 (1984); Ganant et al., "Effect of Estrone Sulfate on Postmenopausal Bone Loss", 76 Obstetrics and Gynecology 529 (1990); all of which are incorporated by reference herein.

In reviewing the examiner's statement of the rejection on pages 4-5 of the Answer, we find that the examiner has failed to come to grips with the key claim limitation that the estrogen is used in an amount of about 0.2 to about 0.8 LED. As seen from page 20 of the specification, the LED of conjugated estrogen is 0.625 mg/day, ethinyl estradiol is 25 micrograms and 7-ß-estradiol is 2 mg/day. Lindsay 1984 confirms that the minimum effective dose of estrogen for preventing bone loss is 0.625 mg/day. To account for that aspect of the claimed invention which requires that estrogen be used in an amount less than the LED, the examiner points to that disclosure in Lindsay 1984 which discusses a dose response curve. For example, in the paragraph bridging pages 761-62, Lindsay indicates that the constructed dose response curve "suggests that 0.45 mg conjugated

equine estrogens per day would exhibit 50% efficacy," which "suggests significant retardation of bone loss would occur at this dose level, although it was not tested."

In considering this aspect of Lindsay 1984, we do not find that it reasonably teaches the administration of less than the LED of an estrogen hormone for the purpose of treating osteoporosis. Reading Lindsay 1984 in its entirety, the reference reasonably suggests that conjugated estrogens would have to be administered in doses of at least 0.625 mg/day in order to be an effective treatment of osteoporosis. As stated in the paragraph bridging pages 761-62 of Lindsay 1984, "all groups of individuals treated with less than 0.625 mg per day showed evidence of bone loss." The portion of Lindsay 1984 relied upon by the examiner refers to a constructed dose response curve and only indicates that the curve "suggests" that 0.45 mg of conjugated equine estrogens per day would exhibit 50% efficacy. As indicated in Lindsay 1984, such low amounts were not tested so that the proposition remains a supposition.

We point to Ettinger, of record, in further support that at the time of the present invention, those of ordinary skill in the art recognized that the LED of conjugated estrogens thought to be useful in preventing osteoporosis was 0.6 mg/day. See the paragraph bridging the columns on page 40 of Ettinger. As set forth in the first full paragraph of the left-hand column of page 44 of Ettinger:

> The dose-response relation for the osteotrophic effect of various estrogens has been evaluated previously, and we have shown that 0.6 mg/d of conjugated estrogens was required to protect oophorectomized women against bone loss (1). Our present study confirms the effectiveness of this

> dosage in women having had spontaneous menopause who have low initial spinal mineral content. Lindsay and associates (4) found 0.6 mg was effective, and Horseman and coworkers (3) showed that ethinyl estradiol, 0.02 mg, a dose equivalent to 0.6 mg of conjugated estrogens, was also the minimum protective dosage. Christensen and associates (2) found that 1 mg of estradiol-17ß, combined with 800 mg of calcium supplementation, was sufficient to maintain bone mineral.

The reference cited in Ettinger as "Lindsay and associates (4)" is Lindsay 1984 relied upon by the examiner in maintaining the rejection under 35 U.S.C. § 103. Ettinger was published in 1987, three years after Lindsay 1984. Thus, to the extent Lindsay 1984 speculated about the effectiveness of a lower dose of conjugated estrogens in treating osteoporosis, workers in the art three years later still considered 0.6 mg/day to be the LED of conjugated estrogens.

We have considered the remaining references relied upon by the examiner but do not find that they teach or suggest the use of from about 0.2 to about 0.8 LED of an estrogen hormone in treating osteoporosis.

The decision of the examiner is reversed.

REVERSED

WILLIAM F. SMITH Administrative Patent Judge	)	
DOUGLAS W. ROBINSON Administrative Patent Judge	)	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
TONI R. SCHEINER Administrative Patent Judge	)	

WFS/cam

David L. Suter
The Procter & Gamble Company
Miami Valley Laboratories
P. O. Box 398707
Cincinnati, OH 45239-8707