

# THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today  
(1) was not written for publication in a law journal and  
(2) is not binding precedent of the Board.

Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

*Ex parte* HANS R. MUELLER,  
MARTIN ULMANN, JOSEF CONTI,  
and GUNTER MUERDEL

Appeal No. 1997-2200  
Application 08/459,692

ON BRIEF

Before KIMLIN, JOHN D. SMITH, and LIEBERMAN, Administrative Patent Judges.

LIEBERMAN, Administrative Patent Judge.

## DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the examiner's refusal to allow claim 7 which is the sole claim in the application.

## BACKGROUND OF THE INVENTION

The diastereomers of folinic acid are known as Leucovorin, or 5-formyl tetrahydrofolate. Folinic acid is also designated as N-(5-formyl-(6R,S)-5, 6, 7, 8-tetrahydro-pteroyl)-L-glutamic acid). Calcium Leukovorin is known as an antidote to folic acid antagonists and is used in cancer treatment. In contrast, the claimed subject matter is distinguishable from the art of record in that it is directed to a compound which is a sodium salt of (6S)-folinic acid having a purity of at least 95%.

## THE CLAIM

Claim 7 is illustrative of appellants' invention and is reproduced below.

7. A sodium salt of (6S)-folinic acid having a purity of at least 95%.

## THE REFERENCES OF RECORD

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

Wood et al. (Wood)	4,959,472	Sep. 25, 1990
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Mueller et al.                      5,347,005                      Sep. 13, 1994  
(Mueller)

Temple et al. (Temple), "Reversal of Methotrexate Toxicity in Mice by a Calcium Salt of Citrovorum Factor and Related Compounds," Cancer Treatment Reports, Vol. 65, Nos. 11-12, pp 1117-1119, Nov./Dec. 1981.

Merck Index, Entry 4111, 10th ed., p. 603, 1983.

Rees et al. (Rees) "Asymmetric Reduction of Dihydrofolate Using Dihydrofolate Reductase and Chiral Boron-Containing Compounds," Tetrahedron, Vol. 42, No. 1, pp. 117-136, 1986.

### THE REJECTIONS

Claim 7 stand rejected under 35 U.S.C. § 103 as being unpatentable over Rees alone or in view of Merck.

Claim 7 stand rejected under 35 U.S.C. § 103 as being unpatentable over Temple alone or in view of Merck.

### OPINION

We have carefully considered all of the arguments advanced by appellants and the examiner and agree with appellants that the aforementioned rejections under 35 U.S.C.

§ 103 are not well founded. Accordingly, we do not sustain the examiner's rejections.

#### ***The Rejection under § 103***

Assuming arguendo that it would have been *prima facie* obvious for one of ordinary skill in the art to prepare appellants' claimed subject matter, it is necessary for us to consider appellants' rebuttal evidence. Appellants urge that they have

presented objective evidence wherein the claimed sodium salt of (6S)-folinic acid has been demonstrated to be unobvious over the corresponding calcium salt. See Brief, pages 3 and 4. We agree. We find the evidence submitted by appellants in the Declarations of Hans Mueller to be dispositive of the issues before us.

As a rebuttal to the *prima facie* case of obviousness, two Declarations by Mueller are submitted. The declarations compare the sodium salt of folinic acid with the calcium salt of folinic acid with respect to their stability over a period of time. In the experiment conducted in the declaration, a marker known only as NP-8, a degradation product of the folinic acid salts, is measured over a period of time. Declarant finds that the increase in the NP-8 content for calcium folinate is three times greater than for sodium folinate. Accordingly, the sodium salt of (6S)-folinic acid has a stability about three times higher than that of the calcium salt. See Brief, page 4, and Declaration of Mueller executed August 9, 1995, page 3.

The examiner's principal objection to the data is that the specification makes no explicit or implicit mention of the property relied on for patentability. Hence, according to the examiner, its consideration is barred as the basic property or utility must be disclosed by appellants in order for affidavit evidence of unexpected properties to be offered. See *In re Davies*, 475 F.2d 667, 670, 177 USPQ 381, 385 (CCPA 1973). See Answer, page 2. Furthermore, the examiner argues that NP-8 has no biochemical significance. See Answer, page 6. However, where the unusual or unexpected results inherently flow from the indicated use of the compound, the property must be considered in determining the patentability of the claimed compound. See *In re Zenitz*, 333 F.2d 924, 927-928, 142 USPQ 158, 161 (CCPA 1964); and

***Ex parte Sasajima***, 212 USPQ 103, 104 (POBA 1981). In the present case, we view the relative stability of a compound as a property that is ordinarily not separable from its disclosed use as a pharmaceutical. Moreover, we determine that the amount of degradant obtained as a result of compound instability is significantly more important than the identity of the degradant. Since we find the stability of the claimed compound to be unusual and unexpected based upon this record, any ***prima facie*** case of obviousness established by the examiner is rebutted and the rejection cannot stand.

For the above reasons, we conclude, evaluating the examiner's ***prima facie*** case of obviousness, if any in view of appellants' evidence and arguments, that based on the totality of the record before us, the preponderance of evidence weighs in favor of non-obviousness within the meaning of § 103. ***In re Oetiker***, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

#### **DECISION**

The rejection of claim 7 under 35 U.S.C. § 103 as being unpatentable over Rees alone or in view of Merck is reversed.

The rejection of claim 7 under 35 U.S.C. § 103 as being unpatentable over Temple alone or in view of Merck is reversed.

The decision of the examiner is reversed.

**REVERSED**

Edward C. Kimlin )  
Administrative Patent Judge )  
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John D. Smith ) BOARD OF PATENT  
Administrative Patent Judge ) APPEALS AND  
 ) INTERFERENCES  
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