

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

\_\_\_\_\_  
BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES  
\_\_\_\_\_

Ex parte FRANCES A. BOUFFARD and JAMES F. DROPINSKI and  
ROBERT A. ZAMBIAS  
\_\_\_\_\_

Appeal No. 95-0976  
Application No. 07/936,558<sup>1</sup>  
\_\_\_\_\_

HEARD: January 16, 1998  
\_\_\_\_\_

Before WINTERS, WEIFFENBACH, and WEIMAR, Administrative Patent Judges.

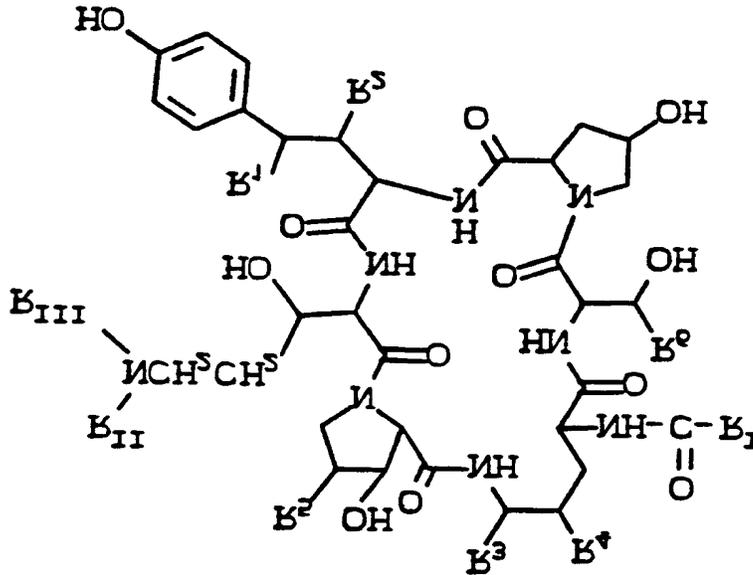
WEIMAR, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal from the examiner's decision finally rejecting claims 1-14. Claims 1 and 13 are illustrative of the subject matter and they read as follows:

\_\_\_\_\_  
<sup>1</sup> Application for patent filed September 3, 1992.

of the said addition salts, and



represented by the formula

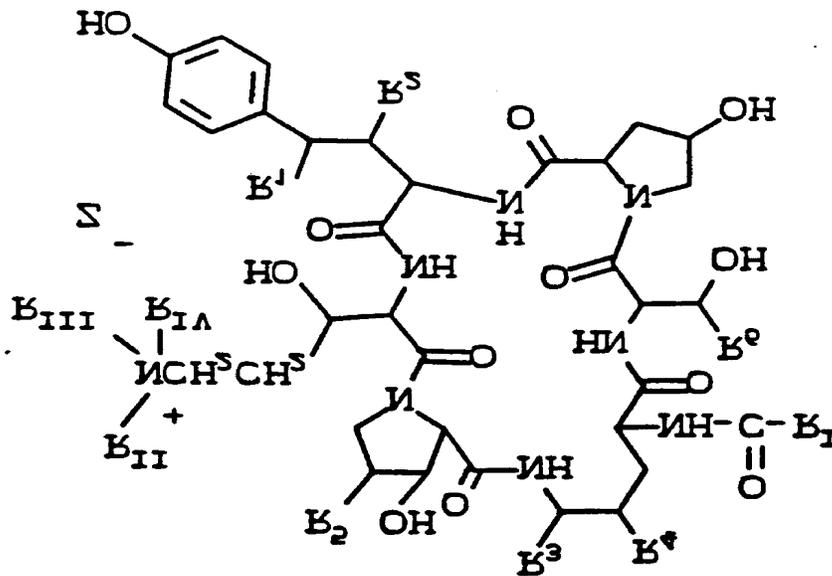
(A) as shown (see ID nos 1-1' 2d)

consisting of:

I. A compound selected from the group

$B_{1A}$  iva  $C^I-C^V$  wtkaj  
 $B_{III}$  foberepei iva  $-(CH^S)^V-$  oi  $-(CH^S)^2-$   
 $B_{III}$  iva H'  $C^I-C^V$  wtkaj oi pousaj oi  $B_{II}$  wpa  
 $B_{II}$  iva H'  $C^I-C^V$  wtkaj oi pousaj  
 wtkoklousbrepaj  
 $C^I-C^{IO}$  wtkoklabrepaj' oi  $C^I-C^{IO}-$   
 $B_I$  iva  $C^d-C^Z$  wtkaj'  $C^d-C^Z$  wtkrepaj' oi  
 $B^e$  iva H oi  $CH^3$   
 $B^2$  iva H' OH oi  $CH^3$   
 $B^v$  iva H oi OH  
 $B^3$  iva  $OC^uH^Zu$  wtkabai'  $OC^uH^Zu$  wtkabai wtkai+ x- oi  
 $B^s$  iva H oi OH  
 $B^j$  iva H oi OH

mpoieiu



nos 1-1' za) iebrebepep pa fpe foimija:  
 (B) w dpaieia wmpoimw wpa (2ed ID

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13. An antibiotic composition comprising therapeutic amount of a compound of Claim 1 in a pharmaceutically acceptable carrier.

The references relied upon by the examiner are:

Sandoz (Belgium)		
'310 Pat.	851,310	Aug. 10, 1977
Sandoz (Belgium)		
'067 Pat.	859,067	Mar. 28, 1978
Schmatz	5,166,135	Nov. 24, 1992

Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure. We reverse this rejection.

Claims 1-14 stand rejected under 35 U.S.C. § 103 over Schmatz or '310 Pat. in combination with '067 Pat. We reverse this rejection.

Claims 1-14 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as lacking patentable distinction over (1) Claims 1-11 and 13 or (2) Claims 1-4 or (3) Claims 3-20 or (4) Claims 4-7 or (5) Claims 1-13 or (6) Claims 1-10 or (7) Claims 1-9 of copending applications (1) 07/936,561; (2) 07/963,332; (3) 07/775,774;

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(4) 07/960,983; (5) 08/005,942; (6) 07/936,434; and (7)  
07/959,948; respectively. We affirm this rejection.

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#### BACKGROUND

Claims 1-12 are drawn to compounds which are derivatives of known cyclohexapeptidyl compounds. These compounds are known in the art as echinocandins. Claims 13 and 14 are drawn to antibiotic compositions comprising the compounds of claim 1.

The compounds that were starting materials for the production of the claimed compounds are echinocandin hexapeptidyl compounds extracted from microbial fermentates. These parent compounds and their antibiotic activity were known prior to the filing date of this application.

#### DISCUSSION

##### Rejection based on 35 U.S.C. § 112

Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph, as having been based on a non-enabling disclosure.

Although phrased various ways the position of the examiner is that the single *in vivo* example of the claimed antibiotic activity is inadequate to provide the necessary guidance to one of skill in the art to practice the invention across the scope of the claim. The claims at issue encompass

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a product claim which is broader than the single compound whose antimycotic activity is exhibited in the specification.

Assuming *arguendo* that the examiner had established a *prima facie* case to reject this claim, the examiner fails to adequately rebut the position taken by appellants. The data presented in the specification on pages 25-29 exhibits antibiotic activity *in vivo* against one strain of yeast and against *Pneumocystis carinii*. However the antibiotic activity of one of the claimed compounds against several strains are shown *in vitro* in this section of the specification. Having shown by animal testing the effectiveness of a compound which exhibited antibiotic properties both *in vitro* and *in vivo*, the appellants' position is that an adequate correlation between *in vitro* test data and *in vivo* test data has been established. The examiner reiterates that one example is inadequate to support many but does not give any reasons why the correlation between *in vitro* and *in vivo* has not been established by the data submitted in the specification.

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Furthermore, appellants take the position that the single compound and the two species tested *in vivo* are adequate representatives of the respective genera of compounds and pathogens. The examiner makes no comment, beyond the statement that the claims cover many species, to controvert the appellants' position.

The appellants also point to the teachings of the applied art (specifically the specifications of the two Belgian patents) for a further showing of the reasonableness of the claimed scope based on similar exhibitions with representative compounds. The examiner's response is to note that in these two publications as well, the *in vivo* data is limited to the use of the same species of yeast as is shown in the instant specification. These patents contain *in vitro* test data which indicate the effectiveness of a representative compound disclosed therein against several genera of mycogenic pathogens.

The examiner has failed to cite references or give specific examples from the prior art or provide scientific reasoning that would counterbalance the reasonableness of the

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position taken by the appellants, and that undue experimentation would not be required for one skilled in the art to practice the claimed invention. Thus, the rejection under 35 U.S.C. § 112, first paragraph is considered to be effectively rebutted and is reversed.

Rejections based on 35 U.S.C. § 103

Claims 1-14 stand rejected under 35 U.S.C. § 103 over Schmatz or '310 Pat. in combination with '067 Pat. We first note that the Examiner's Answer (Paper # 14) fails to provide an explanation of the teachings of each reference relied upon in the obviousness rejection. A previous rejection is not incorporated by reference. The secondary reference, i.e. '067 Pat., is not mentioned in the Examiner's Answer with the exception of its inclusion in the list of references on page 3 and the statement of rejection under 35 U.S.C. § 103 on page 6. Pages 6 and 7 of the Examiner's Answer respond to points raised by appellants in the Brief with respect to the obviousness rejection. Page 10 of the Examiner's Answer contains the following sentence under the heading "(11) Response to argument":

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The issues raised by appellants have been fully responded to under the GROUNDS OF REJECTION, supra.

We are constrained to reverse this rejection in light of the failure of the examiner to present a rejection based on prior art that outlines which teachings are being relied upon to establish the examiner's position that the claims would have been obvious over the cited prior art.

Despite the failure of the Examiner's Answer to present an explanation of the grounds for the rejection under 35 U.S.C.

§ 103, we have reviewed the prosecution history and we will discuss the reasons for rejection which appear at various sites in the record. The presentation of the rejection in the first instance appears in Paper #7 and includes the following points on pages 7 and 8 of that office action:

Each of the compounds of Schmatz or the '310 Pat. differs from the claimed compound in that the claimed compound is a quarternary (sic) ammonium salt derivative of eichinocandin (sic). The Belgian Pat. ('067) however teach (sic) a quarternary (sic) ammonium salt derivative of eichinocandin(sic). (Note page 1, formula 1 of the '067 Pat.). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a quarternary (sic) ammonium salt to the compound of each of Schmatz or '310

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Belgian Pat. as taught by the '067 Pat. with a reasonable expectation that said quarternary (sic) ammonium derivative would exhibit the same or similar antibiotic effect. The claimed compound containing an alkylamine derivative would have been obvious in view of the teachings of the '067 Pat. which appears to teach an alkylamine when n is zero.

On page 6 of the Examiner's Answer the following points are made:

Contrary to appellants' arguments Schmatz teaches an amine at the Thr position. Note col. 18, lines 37-38. Even assuming, for the sake of arguments [sic, argument], that Schmatz does not teach an amine however, it would be within the expected skill of a person in the art to replace the amide i.e., glutamine in the Thr residue of Schmatz with an amine i.e., a basic residue as Orn. Gln and Orn residues belong to the same group of hydrophilic amino acid residues and would reasonably be expected to exhibit similar antibiotic activity. Further, attachment of said amine group in the cyclohexapeptide echinocandin, albeit at different position i.e., at the Orn residue as taught by Schmatz or the Belgian Pat. has been known to exhibit a similar antibiotic effect. To therefore merely transpose or shift a particular substituent to a different location of the peptide sequence, without producing new and unexpected result, would be within the expected skill in the art. Although appellants urge that the Belgian ('310) Pat. discloses only the limited group  $-(CH_2)_{16}-CH_3$  for R5 substituent (RI of the instant application) the said group are (sic) however, within the purview of the claims on appeal.

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Appellants argue that the requirement of the claimed compounds and compositions with respect to the propanolamine substituent at the Thr position is neither taught nor suggested by the applied art. We agree with appellants in this regard. This position being dispositive of the issue of obviousness for each of the claims we will not reach the other questions raised by appellants. We note in particular the issue as to the claimed R<sup>5</sup> position desmethyl variations (set forth in claims 2-12 herein) and point out that the Supplemental Examiner's Answer (Paper #17) refers to variations of echinocandins obtained from a particular microbial source. However, appellants did not file any Reply Brief to address this reasoning. We take no position on this specific matter.

The examiner bears an initial burden of establishing that one of ordinary skill in the art would have found the claimed invention to have been obvious at the time that it was made. The evidence relied upon must support such a conclusion. As was set forth in In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991):

Where claimed subject matter has been rejected

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as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success.

Considering the rejection at issue, with regard to modification of the echinocandin antibiotics taught by Schmatz and '310 Pat. by adding a propanolamine substituent at the Thr position of the cyclic hexapeptidyl compounds, the examiner has taken these positions: 1) that the '067 Pat. appears to teach an alkylamine when n is zero; 2) that Schmatz teaches an amine at the Thr position at col. 18, lines 37-38; 3) that it would be well within the expected skill of a person in the art to replace the amide i.e., glutamine in the Thr residue of Schmatz with an amine i.e., a basic residue as Orn because Gln and Orn residues belong to the same group of hydrophilic amino acid residues and would reasonably be expected to exhibit similar antibiotic activity; and 4) that attachment of said amine group in the cyclohexapeptide echinocandin, albeit at different position

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i.e., at the Orn residue, as taught by Schmatz or the '310 Pat., has been known to exhibit a similar antibiotic effect and to merely transpose or shift a substituent to a different location of the peptide sequence, without producing new and unexpected result would be within the expected skill in the art.

With respect to reason 1), '067 Pat. does not teach an amine substituent at the Thr position when n is zero.

With respect to reason 2), Schmatz teaches at column 18, lines 36-45 that the variable at the Thr position designated  $R^V$  by Schmatz is  $CH_3$ , not an amine. The alkyl amine referred to by Schmatz at column 18, lines 36-45, is substituent  $R^{III}$  which corresponds to  $R_3$  in the compounds claimed herein.

With respect to reason 3), Schmatz does not teach a glutamine in the Thr position. Thus, any thought to replace a glutamine with an ornithine is of no moment. Moreover, such replacement would still fail to create the claimed compounds which retain the hydroxy from the threonine.

With respect to reason 4), the transposition or shifting of a substituent from a specific Orn to a specific Thr in a cyclic hexapeptide does not constitute a variation that is

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obvious on its face. Moreover, to meet the claimed structure one would not be "shifting" the substituent, but duplicating it since the claimed compounds retain alkyl ether amine substituents at the Orn position. Even if one of ordinary skill in the art were to duplicate the substituent at the Orn position it is an ether amine while the claimed substituent alkyl amines at the Thr position are not ethers.

A fundamental flaw in the examiner's reasoning that led to the examiner's conclusion of obviousness is the examiner's reliance on a proposition that making a change is "within the expected skill in the art." As explained by the Federal Circuit in In re Vaeck, *supra*, the obviousness of a claimed compound must be based on the teachings of the prior art and not on whether an artisan of ordinary skill could produce the claimed compounds from compounds known in the prior art. In this case the prior art contains no suggestion that one should make the claimed compounds.

It is well-established that hindsight shall not form the basis of a conclusion of obviousness under 35 U.S.C. § 103. "Both the suggestion and the expectation of success must

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be founded in the prior art, not in the applicant's disclosure."

In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). As the Federal Circuit stated in Sensonics, Inc. v. Aerosonic Corp., 81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996):

To draw on hindsight knowledge of the patented invention, when the prior art does not contain or suggest that knowledge, is to use the invention as a template for its own reconstruction - an illogical and inappropriate process by which to determine patentability. . . . The invention must be viewed not after the blueprint has been drawn by the inventor, but as it would have been perceived in the state of the art that existed at the time the invention was made. [citations omitted]

For the reasons stated above we fail to find a *prima facie* case of obviousness with respect to claims 1-14 based on the art before us.

#### Obviousness-type Double Patenting

Claims 1-14 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting

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as lacking patentable distinction over (1) Claims 1-11 and 13 or (2) Claims 1-4 or (3) Claims 3-20 or (4) Claims 4-7 or (5) Claims 1-13 or (6) Claims 1-10 or (7) Claims 1-9 of copending applications (1) 07/936,561; (2) 07/963,332; (3) 07/775,774; (4) 07/960,983; (5) 08/005,942; (6) 07/936,434; and (7) 07/959,948; respectively.

With respect to application Serial Number 07/960,983 this rejection is now moot in that this application has been abandoned. With respect to application Serial Number 07/775,774 and application Serial Number 07/936,434 this rejection is no longer provisional in that these applications have issued as U.S. Patent # 5,430,018 and U.S. Patent # 5,348,940, respectively.

The Appeal Brief acknowledges this rejection in the paragraph bridging pages 6 and 7, however no argument is presented with respect to the merits of this rejection. In that no arguments have been presented by appellants as to why the examiner's rejection is erroneous, we summarily affirm this rejection.

In the Appeal Brief on page 7, Appellants "request that the Examiner hold any rejection on these grounds in abeyance

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until there is an indication of allowable subject matter."  
Appellants should note that an examiner does not have the  
authority to grant such a request. As explained in the Manual  
of Patent Examining Procedure, MPEP (6th edition, Rev. 3, July  
1997) Section 1206, page 1200-8:

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Appellants must traverse every ground of rejection set forth in the final rejection. Oral argument at the hearing will not remedy such a deficiency in the brief. Ignoring or acquiescing in any rejection, even one based upon formal matters which could be cured by subsequent amendment, will invite a dismissal of the appeal as to the claims affected. If this involves all of the claims, the proceedings in the case are considered terminated as of the date of the dismissal. Accordingly, any application filed thereafter will not be copending with the application on appeal.

In this application we consider appellants' comments to be an acquiescence on the merits. We are loathe to dismiss the appeal given the particular facts of this case, specifically the examiner's handling of the issue. The examiner failed to alert appellants to the consequences of an acquiescence in a rejection and to extend the opportunity to submit a complete Appeal Brief, and the comments made in the Examiner's Answer in this regard, which would give the impression that no more need be said by appellants in relation to the obviousness-type double patenting rejection at this stage of prosecution.

We explicitly state that claims 1-14 are allowable upon the timely filing of a proper Terminal Disclaimer inclusive of all necessary statements with respect to each of the applications and or patents indicated above. Should such

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Terminal Disclaimer(s) be filed the issuance of this application is binding upon the examiner in the absence of new references or other new grounds of rejection. Compare 37 CFR § 1.196(c).

CONCLUSION

The decision of the examiner refusing to allow claims 1-14 under the judicially created doctrine of obviousness-type double patenting is affirmed.

The decision of the examiner refusing to allow claim 1 under 35 U.S.C. § 112, first paragraph, is reversed.

The decision of the examiner refusing to allow claims 1-14 under 35 U.S.C. § 103 is reversed.

The time period in which appellants may file a proper Terminal Disclaimer(s) as noted above is hereby set to expire TWO MONTHS FROM THE DATE OF THIS DECISION.

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

**AFFIRMED**

SHERMAN D. WINTERS	)	
Administrative Patent Judge	)	
	)	
	)	
	)	
	)	BOARD OF PATENT
CAMERON WEIFFENBACH	)	APPEALS
Administrative Patent Judge	)	AND
	)	INTERFERENCES
	)	
	)	
	)	
ELIZABETH C. WEIMAR	)	
Administrative Patent Judge	)	

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ECW/jrg

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APJ WEIMAR

APJ WINTERS

APJ WEIFFENBACH

DECISION: **AFFIRMED**

Typed By: Jenine Gillis

**DRAFT TYPED:** 14 Mar 00

**FINAL TYPED:**