

**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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 13

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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**Ex parte** BRIAN L. DAVIS, PAUL M. CINO  
and LASZLO SZARKA

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Appeal No. 95-4692  
Application 08/141,316<sup>1</sup>

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ON BRIEF

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Before and WILLIAM F. SMITH, **Administrative Patent Judge**,  
MCKELVEY, **Senior Administrative Patent Judge**, and ELLIS,  
**Administrative Patent Judge**.

ELLIS, **Administrative Patent Judge**.

**DECISION ON APPEAL**

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 18, all the claims remaining in the application. Claims 1 and 6 are illustrative of the

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<sup>1</sup> Application for patent filed October 22, 1993.

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subject matter on appeal and are attached as an appendix to  
this  
opinion.

The references relied on by the examiner are:

Terahara et al. (Terahara '227) 1982	4,346,227	Aug. 24,
Terahara et al. (Terahara '859) 1985	4,537,859	Aug. 27,

**American Type Culture Collection (ATCC)**, "Catalogue of  
Bacteria and Phages", Seventeenth edition, pages 16 and 190  
(1989)

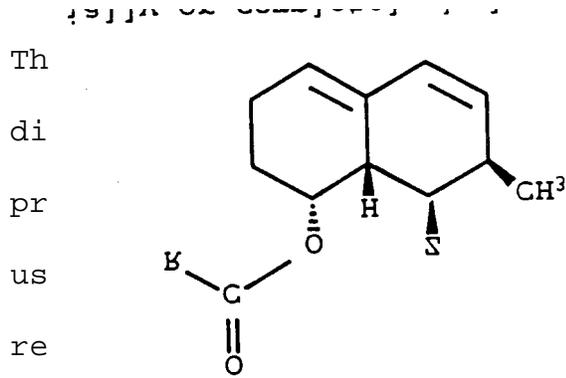
The claims stand rejected as follows:

I. Claims 1 through 18 stand rejected under 35 U.S.C.  
§ 112, first paragraph, as being based on a specification  
which fails to provide an enabling disclosure.

II. Claims 1 through 18 stand rejected under 35 U.S.C.  
§ 103 as being unpatentable over Terahara '227 and Terahara  
'859 and pp. 16 and 190 of the **ATCC** catalogue.

We **reverse**.

### **Background**



(II)' e claimed invention is  
rected to a method of  
eparating "compounds  
eful as HMG-CoA  
ductase inhibitors

and/or intermediates in the preparation of HMG-CoA reductase inhibitors." Specification, p. 1, lines 6-10. The method comprises contacting a compound of the formula:

with a microorganism, selected from the genera *Nocardia*,  
*Amycolata*, *Saccharopolyspora*, *Streptomyces*, *Amycolatopsis*,  
*Saccharothrix* or *Gilbertella*, or with an enzyme derived

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therefrom, or an enzyme having the structure of enzyme derived from said microorganisms, which is capable of catalyzing the hydroxylation of the referenced compound. However, when the referenced compound is compactin, the claimed method excludes the use of microorganisms selected from genera **Nocardia**, **Amycolata** and **Streptomyces**.

**I.**

The examiner argues that the appellants have not demonstrated that the claimed hydroxylation reaction can be performed with an enzyme, nor have the appellants isolated and characterized any enzyme. Answer, p. 3. The examiner further argues that:

The specification does not contain any evidence that the process can indeed be performed by an individual enzyme in a cell free system. Applicant has [sic, applicants have] apparently isolated no enzyme which will accomplish the claimed process and in fact has [sic, have] really not even shown that the process is mono-enzymatic in nature and not in fact cell dependent, hence there is no reasonable expectation that the process is in fact enzymatic. Therefore without any characterization of the enzymatic reaction or enzyme itself, applicant has [sic, applicants have] not enabled claims drawn to the use of an enzyme as it would require undue experimentation by one of ordinary skill in the art at the time

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the invention was made to perform the claimed process in a cell free system. [Answer, pp. 3-4.]

We do not agree with the examiner's arguments.

It is well established that the examiner may reject the claims as being based on a non-enabling disclosure when he has reason to conclude that one skilled in the art would be unable to carry out the claimed invention. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) ("a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirement of the first paragraph of § 112 **unless** there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support"). Here, we do not find that the examiner has applied the appropriate legal standard for determining whether

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a specification provides an enabling disclosure. We caution the examiner that the initial burden lies with him to provide reasons, preferably supported with factual evidence, as to why it would require undue experimentation for one skilled in the art to make and use the invention as claimed. The factors to be considered in determining whether a disclosure would require undue experimentation have been set forth by the court in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In the case before us, we find that the examiner is shifting the burden of proving that the specification provides an enabling disclosure, to the appellants. That is, the examiner is requiring the appellants to provide evidence that the claimed process involves an enzymatic reaction, that it is monoenzymatic in nature, that it is not cell dependent, etc. However, the examiner has not provided any reasons as to why one skilled in the art would have doubted that the claimed method is not enzymatic in nature, or why it would require undue experimentation to perform the claimed process in a cell free system. Moreover, we note that the applied prior art of record teaches the contrary. We direct attention to Terahara '227 and '859 which teach that the hydroxylation of compactin

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is an enzymatic procedure. See, for example, Terahara '227, the abstract; col. 2, lines 21-27. The patents further teach that enzyme-containing extracts can be employed for the hydroxylation procedure. For example, Terahara '227, col. 6, lines 35-37; Terahara '859, col. 19, lines 18-23. In view of the inconsistency between the examiner's arguments and the prior art of record, we reverse the rejection.

## **II.**

The examiner has based his conclusion of obviousness on the teachings of the two Terahara patents and pp. 16 and 190 of the **ATCC** catalogue. Terahara '227 teaches a method of preparing chemical compounds which inhibit the biosynthesis of cholesterol (an HGM-CoA reductase inhibitor; a.k.a., pravastatin) by contacting the compound compactin, or salts and esters thereof, with microorganisms of the genera **Mucor**, **Rhizopus**, **Zygorynchus**, **Circinella**, **Actinomucor**, **Gongronella**, **Phycomyces**, **Martierella**, **Pycnoporus**, **Rhizoctonia**, **Absidia**, **Cunninghamella**, **Syncephalastrum** and **Streptomyces**. Terahara '859 teaches that it is advantageous to use microorganisms of

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the genus ***Nocardia***, over those listed in the '227 patent, because ML-236B (compactin) can be present in the reaction mixture at a much higher concentration.<sup>2</sup> Terahara '859, col. 1, line 63- col. 2, line 8. The **ATCC** catalogue provides a listing of microorganisms within the collection which include, ***inter alia***, ***Amycolata autotropica***, ATCC No. 35204, and ***Saccharothrix australensis***, ATCC No. 31497.

It is the examiner's position that:

It would have been obvious at the time the invention was made for one of ordinary skill in the art to apply the teachings of Terehara [sic, Terahara] and hydroxylyze other known anticholesterolemic compounds (which are structural analogs of compactin) for the medicinal benefits taught by Terehara [sic].

\* \* \*

In fact, it would be [sic, would have been] a matter of judicious choice and thus obvious to the skilled artisan to select other microorganisms which would work in the reference [sic, referenced] process. The teachings of the reference are so broad that they would have to be considered general teachings as the reference teaches a multitude of microorganisms capable of such hydroxylation reactions. Given this

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<sup>2</sup> According to Terahara, the ML-236B compound possesses antifungal and antibiotic properties. Terahara '859, col. 2, lines 5-8.

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general teaching, it would have been well within the purview of the skilled artisan to perform the microbial process of the references using other microorganisms which are closely related to those used in the reference. The teachings of the Terehara [sic] references, given their breadth, provide the skilled artisan with a reasonable expectation that the closely related micro-organisms will function in a like manner and perform the conversion [Answer, pp. 5-6].

We find this position untenable.

It cannot be gainsaid that the examiner has the burden under § 103 to establish a **prima facie** case of obviousness.

**In re Fine**, 837 F.2d 1071, 1074-76, 5 USPQ2d 1596, 1598-1600 (Fed. Cir. 1988); **In re Piasecki**, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984). To that end, the examiner must show that some objective teaching or suggestion in the applied prior art, or knowledge generally available in the art, would have led those of ordinary skill to combine the teachings of the references to arrive at the claimed invention. **Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.**, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed. Cir. 1996); **In re Fritch**, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992); **In re Fine, supra**; **Ashland Oil, Inc. v. Delta Resins & Refractories**,

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*Inc.*, 776 F.2d 281, 297 n. 24, 227 USPQ 657, 667 n. 24 (Fed. Cir. 1985), **cert. denied**, 475 U.S. 1017 (1986). It is impermissible for the examiner to use the applicants' specification as an instruction manual or template to piece together the teachings of the prior art. *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531-32 (Fed. Cir. 1988).

In the case before us, the examiner's overall position is that since one of ordinary skill in the art routinely synthesizes pravastatin by contacting certain genera of microorganisms<sup>3</sup> with compactin, esters or salts thereof, it, therefore, would have been obvious to such persons to produce pravastatin by contacting any genera of microorganism with compactin, or analogs thereof. However, from a fair reading of the references relied upon by the examiner, it is difficult for us to discern on what basis this conclusion was reached.

In our view, the teachings of the Terahara patents are

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<sup>3</sup> *Viz.*, *Mucor*, *Rhizopus*, *Zygorynchus*, *Circinella*, *Actinomucor*, *Gongronella*, *Phycomyces*, *Martierella*, *Pycnoporus*, *Rhizoctonia*, *Absidia*, *Cunninghamella*, *Syncephalastrum*, *Streptomyces* and *Nocardia*.

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directed to the use of specific genera of microorganisms and specific substrates. We do not find, nor has the examiner pointed out, any teachings in the Terahara patents which would have suggested to those of ordinary skill in the art, the use of the claimed genera of microorganisms to produce pravastatin from compactin or the claimed analogs. On this record, the only place we find such a suggestion is in the appellants' specification. Thus, in our view, the examiner has relied on impermissible "hindsight" to arrive at the conclusion that the present invention is obvious over the prior art. ***In re Fritch, supra; Interconnect Planning Corp. v. Feil***, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps").

Accordingly, the rejection is reversed.

#### ***Other Issues***

Upon return of this application to the corps, the examiner should reconsider whether there is a factual basis

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for finding that the specification fails to provide an enabling disclosure with respect to the claimed enzymes. In so doing, the examiner should bear in mind the appropriate legal standard discussed above. **See *In re Marzocchi, supra***. Also, the test for enablement is whether one skilled in the art could make or use the claimed method from the teachings in the specification, coupled with information from the art, without undue experimentation. Undue experimentation is not determined by a single factual inquiry, rather, it is a finding which is made after weighing several factors. **See *In re Wands***, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) ("Factors to be considered in determining whether a disclosure would require undue experimentation . . . include (1) the quantity of experimentation necessary, (2) the amount and direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims").

As for the case before us, we acknowledge that the

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specification does not describe the characterization of any microbial enzymes which are derived from the claimed microorganisms and which are capable of catalyzing the hydroxylation of compactin or analogues thereof. Nor does the specification describe the characterization of any enzymes having the structure of said microbial enzymes and which are capable of catalyzing the claimed hydroxylation reaction. In considering whether it would require undue experimentation for those skilled in the art to "make and use" the claimed method, the examiner should consider such facts in light of the various factors set forth by the court in *In re Wands, supra*. For example, what was the state of the art at the time the application was filed? Was the hydroxylation of compactin and analogs thereof well known in the art? Was this a known and well characterized pathway at the time the application was filed? Were the enzyme(s) involved known and characterized? How much guidance does the specification provide as to the isolation and characterization of such enzyme(s)? How many working examples of the claimed enzyme(s) does the specification provide? Is the structure of the claimed enzyme(s) predictable based on the teachings of the specifi-

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cation, or knowledge generally available in the art? Would the isolation of an enzyme having the claimed properties require extensive or routine experimentation? **Etc.**

In making his evaluation, the examiner should also consider the guidance recently provided by our appellate reviewing court in **Genentech, Inc. v. Novo Nordisk, A/S**, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997):

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. **See Brenner v. Manson**, 383 U.S. 519, 536, 86 S. Ct. 1033, 1042-43, 16 L.Ed.2d 69, 148 USPQ 689,696 (1966)(stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

In reconsidering the issue of enablement, the examiner is urged to take all of the foregoing into account. If the examiner determines that the claims on appeal would not have

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been enabled throughout their scope, he may -if he be so  
advised- reopen prosecution and institute a fact-based  
rejection.

**REVERSED**

	WILLIAM F. SMITH	)	
	Administrative Patent Judge	)	
		)	
		)	
	FRED E. MCKELVEY	)	BOARD OF
PATENT	Senior Administrative Patent	)	APPEALS AND
	Judge	)	INTERFERENCES
		)	
		)	
	JOAN ELLIS	)	
	Administrative Patent Judge	)	

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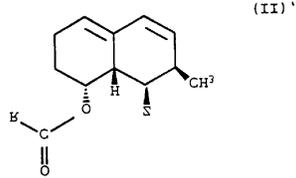
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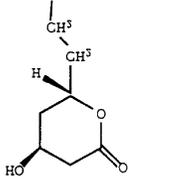
**APPENDIX**

γνώσεως, γνώσεως οκ ερεθισμους.  
 εμε συνουμ οξ εοκμης II τσ συνθεστυμ, εμε πηκκοοιδσντμ τσ νοφ  
 γνωσησσοβετσ, εσσομστοσμτμ οκ εττρεεεττμ, ελολτρεφ εμτμ μπεν  
 νοσσεττμ, γνωσησσε, εσσομστοβοττλοβε, ερεθισμους.

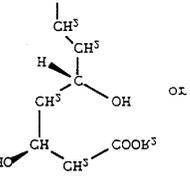
μπεε εστμ πηκκοοιδσντμ τσ εεεεεφ ετωμ εμε δευεττ  
 I οκ εεττ εμεεοξ, εμ εττεεεττμ εεττ μλκροκλττρεττμ.  
 εοκμης II οκ εεττ εμεεοξ εο λττμ εεττ συνουμ οξ εμε εοκμης  
 σθεεττ οξ σθεεττλττμ εμε μλκροκλττρεττμ οξ εεττ συνουμ οξ εμε  
 εεεεεττ οξ εμ εμλμε εεττ ετωμ, εεττ πηκκοοιδσντμ, μττμ τσ  
 πηκκοοιδσντμ, οκ μττμ εμ εμλμε εεττ ετωμ, οκ μεεττμ εμε  
 εμεεοξ, μπεεττμ ε' ε εμ εε  
 ε εεεεεττμ οκ σμπεεεεττμ μλκροδενεεεφ εττμ εμεττμ οκ ε εεττ



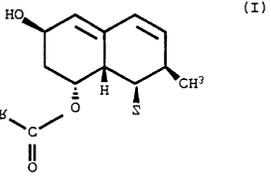
εοκμης II:  
 σμπεεεεττμ εμε εεεε οξ σμπεεεεττμ ε συνουμ οξ εμε  
 μεεεττ:  
 εε τσ μλκροδεν, εττκλτ, εμμμμττμ, εττκλτ-εμμμμττμ οκ εττκλτ  
 ε εμ



εμε τσ εεεε



ε τσ εμε οδεν σμεττμ μμττεεε  
 ε τσ εττκλτ οκ εττκλτ:  
 εμεεοξ, μπεεεττμ  
 ττσ εεεεεττμ οκ σμπεεεεττμ μλκροδενεεεφ εττμ εμεττμ οκ ε εεττ



εοκμης I:  
 τ. ε μεεμμ ετωμ εμε εεεεεεεεεττμ οξ ε συνουμ οξ εμε

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ՀԱՐՑԱԿՈՑՈՒՄԻ ԵՆԿՐՈՒՄԵՆ ԱՄԸ ԴԵՅՅ՝  
ԱՄԸ ՆԻՑԻՆ՝ ՀԱՐՑԱԿՈՑՈՒՄԻ ԽՐԱՄԵՆ ԱՄԸ ՆՕՉՕՂ ՕՒ  
ՀԱՐՑԱԿՈՑՈՒՄԻ ԽՐԱՄԵՆ ԱՄԸ ՆԻՑԻՆ՝ ՀԱՐՑԱԿՈՑՈՒՄԻ ԽՐԱՄԵՆ  
ՏՈՒՆԵՆԵՆԻՆ ԱՄԸ ՆԻՑԻՆ՝ ԵՐԵՎԱՆԻ ԲԵՐԻՏՈՒՄԻ ԱՄԸ ՆՅՅՅՂ՝  
ԴՅՅՅ՝ ԱՄԸՆԵՐՈՒՄԻ ՄԵՐԵՎՈՒՄԻ ԱՄԸ ՆԻՑԻՆ՝ ՀԱՐՑԱԿՈՑՈՒՄԻ  
ԱՄԸՆԵՐՈՒՄԻ ՏՈՒՆԵՆԵՆԻՆ ԱՄԸ ՆՅՅՅՂ՝ ԵՐԵՎԱՆԻ ԵՐԵՎԱՆԻ ԱՄԸ  
Ե՝ ԴԵ ՄԵՐՈՒՄ ԵՐ ԵՐԻՆ Ե՝ ԵՐԵՎԱՆԻ ԵՐԵՎԱՆԻ ԱՄԸ