

**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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 34

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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*Ex parte* ANTHONY MARFAT  
and RALPH P. ROBINSON

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Appeal No. 95-1618  
Application 08/033,456<sup>1</sup>

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ON BRIEF

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Before JOHN D. SMITH, WEIFFENBACH and ELLIS, *Administrative Patent Judges*.

WEIFFENBACH, *Administrative Patent Judge*.

**DECISION ON APPEAL**

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-6 and 8-13 which are all of the claims remaining in the application. We reverse.

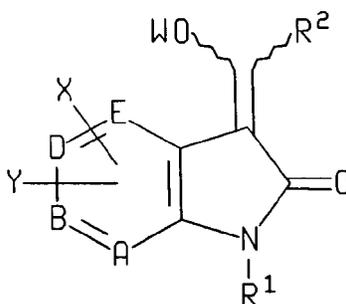
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<sup>1</sup> Application for patent filed March 18, 1993. According to applicants, this application is a continuation of Application 07/960,208, filed October 13, 1992, now abandoned, which is a continuation of Application 07/846,756, filed March 5, 1992, now abandoned, which is a continuation of Application 07/612,054, filed November 9, 1990, now abandoned.

### The Claimed Subject Matter

The claims on appeal are directed to 4-, 5-, 6-, and 7-azaoxindole derivatives which according to appellants are useful, *inter alia*, in the prevention or treatment of chronic inflammatory diseases, allergy, psoriasis, various bone diseases, and immune dysfunctions such as systemic lupus erythematosus. Claim 1 is representative of the claimed subject matter and is reproduced below.

1. A compound of the formula



wherein one of A, B, D and E is N and the others are CH; X and Y are independently selected from hydrogen, OR<sup>3</sup>, hydroxy, (C<sub>1</sub>-C<sub>6</sub>) alkyl, CF<sub>3</sub>, COR<sup>3</sup>, halogen, C<sub>0</sub>OR<sup>3</sup>, CONR<sup>3</sup>R<sup>3</sup>, CN, NO<sub>2</sub>, SR<sup>3</sup>, SOR<sup>3</sup>, SO<sub>2</sub>R<sup>3</sup> and SO<sub>2</sub>NR<sup>3</sup>R<sup>3</sup>; R<sup>1</sup> is (C<sub>1</sub>-C<sub>6</sub>) alkyl or CONHR<sup>4</sup>; R<sup>2</sup> is (C<sub>1</sub>-C<sub>8</sub>) alkyl, (CH<sub>2</sub>)<sub>n</sub>R<sup>5</sup> wherein n is 0 or 1, or NHR<sup>8</sup>R<sup>3</sup> is (C<sub>1</sub>-C<sub>6</sub>) alkyl, phenyl, benzyl, allyl or hydrogen, wherein said phenyl and the phenyl moiety of said benzyl may optionally be substituted with one or more substituents independently selected from fluoro, chloro, bromo, iodo, hydroxy, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy and CF<sub>3</sub>; R<sup>4</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>8</sub>) cycloalkyl, COR<sup>3</sup> wherein R<sup>3</sup> is as defined above, phenyl, substituted phenyl, heteroaryl or substituted heteroaryl, wherein the heteroaryl moiety of each of said heteroaryl and substituted heteroaryl groups is selected from thiophene and furan, and wherein each of said substituted phenyl and substituted heteroaryl groups is substituted with one or two substituents independently selected from fluoro, chloro, bromo, iodo, hydroxy, (C<sub>1</sub>-C<sub>3</sub>) alkyl, (C<sub>1</sub>-C<sub>3</sub>) alkoxy and CF<sub>3</sub>; R<sup>5</sup> is (C<sub>3</sub>-C<sub>8</sub>) cycloalkyl, hydrogen, phenyl, substituted phenyl, heteroaryl and substituted heteroaryl, wherein the heteroaryl moiety of each of said heteroaryl and substituted heteroaryl groups is selected from thiophene and furan, and each of said substituted phenyl and substituted heteroaryl groups is substituted with one or two substituents independently selected from fluoro, chloro, bromo, iodo, hydroxy, (C<sub>1</sub>-C<sub>3</sub>) alkyl, (C<sub>1</sub>-C<sub>3</sub>) alkoxy and trifluoromethyl; R<sup>6</sup> is phenyl, thiophene or furan, wherein said phenyl, thiophene and furan may be optionally substituted with one

or more substituents independently selected from fluoro, chloro, bromo, iodo, hydroxy, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>3</sub>) alkoxy and thiofluoromethyl; and W is hydrogen, (C<sub>2</sub>-C<sub>10</sub>) alkanoyl, (C<sub>3</sub>-C<sub>7</sub>) cycloalkylcarbonyl, (C<sub>7</sub>-C<sub>10</sub>) phenylalkanoyl, chlorobenzoyl, thenoyl, omega-(C<sub>2</sub>-C<sub>4</sub>)-alkoxycarbonyl-(C<sub>3</sub>-C<sub>5</sub>)alkanoyl, (C<sub>2</sub>-C<sub>10</sub>)alkoxycarbonyl, phenoxycarbonyl, 1-[(C<sub>1</sub>-C<sub>4</sub>)acyloxy]-(C<sub>2</sub>-C<sub>4</sub>)alkyl, 1-[(C<sub>2</sub>-C<sub>5</sub>)alkoxy-carbonyloxy]-(C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)-alkylsulfonyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, methylphenylsulfonyl and di-(C<sub>1</sub>-C<sub>3</sub>)alkyl phosphonate; with the proviso that (a) when E is nitrogen, then at least one of X and Y is other than hydrogen; (b) when either R<sup>2</sup> is NHR<sup>6</sup> or R<sup>1</sup> is (C<sub>1</sub>-C<sub>6</sub>)alkyl, then W is hydrogen; or a pharmaceutically acceptable salt thereof.

### The Rejections<sup>2</sup>

I. Claims 1-6 and 8-13 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that (i) certain amendatory subject matter to the specification in an amendment filed October 15, 1993 (Paper No. 25) constitutes new matter in that “by deletion of selected language from the specification and insertion of new formula designations appear to be expanding the scope of the original disclosure whereby new matter is introduced...,” and (ii) the specification fails to provide an adequate written description of the invention and fails to adequately provide an enabling disclosure for the following reasons as stated in the final rejection (Paper No. 26, pp. 3-4):

Applicants\* specification fails to clearly distinguish between tautomer structures. It is not clear which tautomers are intended. The originally filed disclosure appeared to intend a limited scope of tautomer structures however pursuant to applicants\* amendment of 10-15-93 a different broader scope appears to

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<sup>2</sup>In the final rejection, the examiner rejected claim 8 on the ground that the formula in claim 8 did not have support in the original disclosure. The examiner withdrew this rejection in view of appellants’ “suggestion to amend the Formula in claim 8 so as to recite a hydroxyl group (instead of a single bonded oxygen)” (Answer, p. 2). Appellants suggested amending “the structure of claim 8 such that the oxygen in the 3- position is bonded to a hydrogen since it would be obvious to one of ordinary skill in the art that said compound as it presently stands would have that chemical structure” (Brief, p. 1). Appellants also presented a table in the Brief providing page and line numbers in the specification as originally filed for support for the formula in claim 8 (Brief, pp. 4-7). It appears to us that despite the suggestion made by appellants which prompted the examiner to withdraw this portion of the rejection, the specification on page 6, line 25, as well as original claim 1, provides support for the formula in claim 8. Both disclose that W can be hydrogen.

be intended. In either case the specification is unclear and fails to point out with particularity the claimed invention to the skilled artisan in such a way that it can [be] made and used without undue experimentation. The purpose [of the] specification is to objectively enable the claimed invention. Applicants [sic, Applicants'] specification appears to only indicate to the skilled artisan the area of subject matter wherein it would be obvious to try to find the invention. It would require undue experimentation on the part of the skilled artisan to define the true scope of the claimed invention and reduce it to practice.

Applicants\* disclosure is conspicuously devoid of any specific recitation of examples that would be considered necessary in the instant case to objectively enable the invention, i.e. teach one of ordinary skill how to make all the disclosed tautomers and/or isomer\*s [sic, isomers]. There are multiple sets of tautomers and geometric isomers theoretically possible for Formula I [on page 5 of the specification, which is the same formula recited in claim 1, *supra*]. There is no reason to believe that all of these variations are sufficiently stable, [and] can be made or have the alleged utility in view [of the] inherent structural differences. Furthermore, the examiner maintains the position that the originally filed specification fails to adequately specify what is encompassed by Formula I or clearly specify the true scope of the invention. Even when considering applicants\* amendments which introduce new mater [sic, matter], the specification remains unclear as to the metes and bounds of the invention intended to be disclosed.

Each part of the rejection is prefaced on an objection to the specification.

II. Claims 5, 6, 12 and 13 stand rejected under 35 U.S.C. §§ 101 and 112, first paragraph, on the ground that there is “insufficient data in the specification to show that the claimed pharmaceutical composition is therapeutically effective in the treatment of the various complications and diseases disclosed” (Paper No. 26, p. 5).<sup>3</sup>

### **Opinion**

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<sup>3</sup>This rejection has not been restated or referred to in the Answer by the examiner. Appellants' identified the rejection as Issue IV and presented arguments traversing the rejection. The examiner responded to these arguments. It is, therefore, presumed that the examiner's failure to restate the rejection was an oversight and that the rejection is viable and has not been withdrawn.

On October 15, 1993, appellants filed an amendment which the examiner objects to as introducing new matter into the specification and broadening the scope of the disclosure. The examiner objects to the designation of formula I at the bottom of page 12 and at page 16, line 1 as “Ir”, formula I at the bottom of page 14 as “Irr,” and formula I at the bottom of page 15 as “Irrr.” According to the examiner, these changes expand the scope of the original disclosure. Appellants argue that by introducing of the prime symbols, they in no way broadened the original disclosure or introduced new matter since formulas Ir, Irr and Irrr are subgenres of formula I on page 5 of the specification. The examiner, however, does not consider the formulas Ir, Irr and Irrr to be subgenus compounds, but tautomers and/or isomers of formula I. The examiner asserts in response to appellants’ arguments in the Brief that appellants are “confusing” the terms subgenus with tautomers or isomers.

The examiner also objects to the amendment at page 10, line 34 to page 11, line 8 of the specification which was amended as follows (the subject matter deleted which is at issue is enclosed in brackets and is presented in bold type for emphasis):

The compounds of formula I exist in several tautomeric forms, due to the presence of the carbonyl carbon at position 2 on the azaoxindole ring and the acyl carbon attached to the carbon at position 3 of the ring. Such compounds also exist as geometric isomers of the tautomeric structure in which a double bond exists **[between the nitrogen at position 1 and the carbon at position 2 of the ring]**. This invention relates to all tautomeric forms and geometric isomers of the compounds of formula I.

The examiner considers the deleted subject matter “as broadening the scope of the disclosure and thus introduce new matter” (Paper No. 26, p. 1). Appellant argues that the specification as originally

filed discloses that the “invention relates to all tautomeric forms and geometric isomers of compounds of formula I.”

The new matter objections raised by the examiner in the final rejection as per the October 15, 1993 amendment are not properly before us. While we are of the opinion that the addition of the prime symbols help to distinguish between various subgenus compounds of the formula I set forth on page 5 of the specification, the examiner has not shown how the new matter objection affects the claims on appeal.<sup>4</sup> By virtue of the fact that claims 1-6 are original patent claims, the underlying concept of the written description requirement of the first paragraph of 35 U.S.C. § 112 has been satisfied as to these claims. *In re Smith*, 482 F.2d 910, 914, 178 USPQ 620, 624 (CCPA 1973). As for claims 8-13 which were added later in the prosecution, the examiner has the initial burden of presenting evidence or reasoning as to why one of ordinary skill in the art would not have recognized in the specification a description of the invention as later claimed in these claims. On this record, the examiner has not met his burden. Accordingly, the new matter objections raised by the examiner are petitionable matters, and not new matter issues reviewable by appeal to the Board of Patent Appeals and Interferences. Accordingly, we will not consider the new matter issue as it pertains to the amendments to pages 10-12 and 14-16 of the specification. To the extent that the rejection of the

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<sup>4</sup> Section 608.04(c) of the Manual of Patent Examining Procedure, 6th Edition, Rev. 3, July 1997, states in part, that

[w]here the new matter is confined to amendments to the specification, review of the examiner's requirement for cancellation is by way of petition. But where the alleged new matter is introduced into or affects the claims, thus necessitating their rejection on this ground, the question becomes an appealable one, and should not be considered on petition even though that new matter has been introduced into the specification also.

appealed claims is based on the written description requirement of 35 U.S.C. § 112, it is reversed.

As for ground (ii) of the rejection under the first paragraph of 35 U.S.C. § 112, the examiner asserts that “Applicants’ disclosure is conspicuously devoid of any specific recitation of examples that would be considered necessary in the instant case to objectively enable the invention, i.e. teach one of ordinary skill how to make all the disclosed tautomers and/or isomers” and that undue experimentation would be required for one skilled in the art “to define the true scope of the claimed invention and reduce it to practice” (Paper No. 26, p. 4). We find that the rejection lacks merit. First, we note that the written description requirement is separate from the enablement requirement. See *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991); *In re Wilder*, 736 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1984), *cert. denied, sub nom. Wilder v. Mossinghoff*, 469 U.S. 1209 (1985); *In re Barker*, 559 F.2d 588, 591, 194 USPQ 470, 472 (CCPA 1977), *cert. denied, sub nom. Barker v. Parker*, 434 U.S. 1238 (1978). The rejection before us appears to be grounded only on lack of enablement, i.e. how to make and use the invention, and not on an inadequate written description of the claimed invention because the examiner has not shown that the alleged failure to present working examples in the disclosure of the application as originally filed would have reasonably conveyed to a person having ordinary skill in the art that the inventors did not have possession at that time of later claimed subject matter. *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983). Second, the examiner’s assertions of lack of enablement and undue experimentation are conclusional in nature. The examiner has not presented any objective evidence and/or scientific reasoning to explain why undue experimentation would be

required to make and use the claimed invention. *In re Scarbrough*, 500 F.2d 560, 566, 182 USPQ 298, 303 (CCPA 1974); *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971). The examiner has not explained how and why appellants' detailed description of how to make the claimed compounds described on pages 11-31 and in the 56 examples of the specification would not have enabled one skilled in the art to make and use the claimed invention without undue experimentation and why one skilled in the art would find it necessary for applicant to disclose how to make all tautomers and isomers of formula I in order to comply with the enablement requirement. For the foregoing reasons, the rejection of claims 1-6 and 8-13 under the first paragraph of 35 U.S.C. § 112 is reversed.

The examiner also rejected claims 5, 6, 12 and 13 under 35 U.S.C. §§ 101 and 112, first paragraph, for the following reasons (Paper No. 26, pp. 5-6):

There is insufficient data in the specification to show that the claimed pharmaceutical composition is therapeutically effective in the treatment of the various complications and diseases disclosed. The specification is devoid of any data for in vitro or in vivo tests. When [the] disclosed utility is the production of a physiological response, the dosage effective to achieve this response in a host, whether human or animal, must be disclosed, *In re Gardner et al.* (CCPA 1970) 427 F.2d [sic, F.2d] 786, 166 USPQ 138. Some showing of empirical results is necessary to establish the utility of a method of treating or preventing using [sic] applicants' compositions. For instance the prevention of autoimmune diseases, (i.e. such as AIDS) raises the issue of prima facie incredible utility. Lack of evidence of the effectiveness of the claimed method of treating cancer [or autoimmune diseases such as AIDS] coupled with an experimental paper protocol as the relevant working example can justify a rejection under both 35 U.S.C. § 101 and § 112. *Ex parte Stevens* (BPAI 1990) 16 [US]PQ2d 1379. Applicants' claimed invention is sufficiently unusual to warrant requiring substantiating evidence, *Ex parte Busse et al.* (BPAI 1986) 1 [US]PQ2d 1908.

It is not clear from the disclosure that [a] useful activity has been determined or demonstrated in fact for the plurality of possible compounds encompassed by the

Formula I. Said plurality of possible compounds have a multitude of divergent chemical functionalities which would be expected to effect observed physical properties important to pharmacological utility. Applicants' own argument of 3-18-93 is that the mere substitution of a nitrogen atom for a carbon atom in a core oxindole structure to produce the corresponding azaoxindole would not be expected to result in similarly useful compounds. Thus, similar or more drastic differences between species encompassed by applicants' generic disclosure would necessitate proof of utility beyond a mere allegation since common utility would not be expected by one of ordinary skill.

Appellants argue that there is support for utility throughout the specification. They point to the abstract and written description of the invention which refer to the compounds of the invention as being useful as antiinflammatory and analgesic agents; as inhibitors of prostaglandin H<sub>2</sub> synthase, 5-liposygenase, and interleukin-1-biosynthesis; and for the treatment of chronic inflammatory diseases, allergy, psoriasis, various bone diseases, and immune dysfunctions such as systemic lupus erythema-tosis. They also refer to a detailed assay procedure set forth in the specification at page 31, line 15 to page 34, line 40 showing the ability of the claimed compounds to inhibit interleukin-1 biosynthesis, prostaglandin H<sub>2</sub> synthase, and 5-lipoxygenase, and to page 35, lines 4-15 for a demonstration of the antiinflammatory and analgesic activity of the claimed compounds.

In response to appellants' arguments in the Brief, the examiner states he "doubts the objective truth" the utility asserted by appellants. On page 8 of the Answer, the examiner states that his doubt is

based on the fact that the compounds encompassed by the language "all tautomers and geometric isomers of the compounds of formula I" are sufficiently different so that one of ordinary skill would not expect them to have the same pharmacological properties and therefore would not expect these compound to have the alleged utility attributed to the compounds of formula I. Appellants' arguments regarding utility are

mere allegations that are unsupported by facts or evidence. Saying so does not make it so! There does not appear to be a single instance in the specification teaching one of ordinary skill how to use any single specific compound or how to treat or prevent any one of the plurality of alleged deceases [sic, diseases]. It is not the purpose of the disclosure to simply direct one of ordinary skill to the area of research where the invention may be found or indicate what would be obvious to try. The purpose of the disclosure is to set forth the invention in such clear and precise terms so as to teach the skilled artisan how to make and use the invention without having to resort to undue experimentation.

\* \* \*

Appellants proffer that by an assay procedure the ability of the compounds of formula I to inhibit interleukin-1 biosynthesis may be determined. Appellants' specification points to a broad area of subject matter wherein it might be obvious to try to find the invention. It would require more than reasonable and routine experimentation to make all the compounds encompassed by the claimed invention and then ferret out the practical embodiments and reduce them to practice.

\* \* \*

There is no evidence presented which clearly and reproducibly illustrates that there is any utility for the claimed invention. There is no suggestion that any of the disclosed utilities are attainable. Applicants' claimed utility is generic in nature and relates to [a] method of treatment by inhibiting a metabolic pathway. In order to satisfy the requirement of utility, there must be disclosed [an] ultimate use and a linkage between a claimed metabolic pathway and each disease and/or diseases disclosed in the specification.

After consideration of appellants\* arguments and the examiner\*s position, we do not find the examiner's rejection to be sustainable. Applicants' statements of utility are not mere allegations, but must be taken by the examiner as being true unless the examiner can present evidence and/or scientific reasoning to cast reasonable doubt as to the utility of the compounds being asserted by applicants. In the case before us, the examiner has not presented any factual showing or a detailed analysis of the

appellant\*s disclosed assay procedures and demonstrations of antiinflammatory and analgesic activity of the claimed compounds to establish that a person skilled in the art would have reasonably concluded that none of the asserted utilities are credible. The mere identification of a single pharmacological activity use which provides an immediate benefit to the public satisfies the utility requirement. *Nelson v. Bowler*, 626 F.2d, 853, 856, 206 USPQ 881, 883 (CCPA 1980). In this case, appellants' statement that the claimed compounds have several pharmacological activities would clearly provide an immediate benefit to the public, such as being used as an antiinflammatory and analgesic agent and for the treatment of chronic inflammatory diseases, psoriasis, and immune dysfunctions such as systemic lupus erythematosus.

The examiner\*s statements regarding the deficiencies of the specification as lacking a disclosure of *in vitro* and *in vivo* tests, lack of a showing of empirical results, and lack of evidence of effectiveness of the claimed compounds are all conclusional in nature and are not corroborated by evidence or scientific reasoning. As for the examiner\*s conclusion that the plurality of possible compounds encompassed by the claimed subject matter would not have the utility asserted by appellants, the examiner has made broad sweeping statements without presenting any factual evidence or analysis of appellants\* disclosure to support his conclusion. The examiner has not presented any factual showing or analysis of appellants\* disclosed examples, assay procedures, and demonstration of pharmacological activity which would cause a person having ordinary skill in the art to reasonably doubt the objective truth of appellants\* statements of asserted utility. Accordingly, we find that appellants\* disclosure of utility satisfies 35 U.S.C. § 101 and meets the enablement requirement of

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the first paragraph of 35 U.S.C. § 112.

For all of the foregoing reasons, the examiner s rejections are reversed.

**REVERSED**

JOHN D. SMITH	)	
Administrative Patent Judge	)	
	)	
	)	BOARD OF PATENT
	)	) APPEALS AND
CAMERON WEIFFENBACH	)	INTERFERENCES
Administrative Patent Judge	)	
	)	
	)	
	)	
JOAN ELLIS	)	
Administrative Patent Judge	)	

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