

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. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte FRANCESCO DELLA VALLE and
AURELIO ROMEO

Appeal No. 1999-1417
Application 08/268,730

HEARD: July 12, 2001

Before WINTERS, WILLIAM F. SMITH, and SCHEINER, Administrative Patent Judges.
WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 74 and 76 through 80. Claims 75 and 81, which are the only other claims remaining in the application, stand objected to as depending from a rejected claim but would be allowable if rewritten in independent form. See the Advisory Action, Paper No. 29, mailed August 12, 1996.

Representative Claims

Claims 74 and 76, which are illustrative of the subject matter on appeal, read as follows:

74. A pharmaceutical composition containing, as active ingredient, an N-acyl-lysoganglioside wherein the acyl group is derived from an aliphatic acid having from 2 to 12 carbon atoms, substituted with at least one polar group selected from the group consisting of

chlorine and fluorine and etherified hydroxy groups

or esters or amides of the sialic carboxy groups of said N-acyl-lysogangliosides, inner esters of said N-acyl-lysogangliosides, peracylated derivatives of said N-acyl-lysogangliosides, metal salts or organic base salts of said N-acyl-lysogangliosides having acid groups, acid addition salts of said N-acyl-lysogangliosides and mixtures of said N-acyl-lysogangliosides, together with a pharmaceutically acceptable excipient.

76. A method of treating disorders related to excitatory amino acid-induced neurotoxicity wherein an N-acyl-lysoganglioside wherein the acyl group is derived from an aliphatic acid having from 2 to 12 carbon atoms, substituted with at least one polar group selected from the group consisting of

chlorine and fluorine and etherified hydroxy groups

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or esters or amides of the sialic carboxy groups of said N-acyl-lysogangliosides, inner esters of said N-acyl-lysogangliosides, peracylated derivatives of said N-acyl-lysogangliosides, metal salts or organic base salts of said N-acyl-lysogangliosides having acid groups, acid addition salts of said N-acyl-lysogangliosides and mixtures of said N-acyl-lysogangliosides is administered to a patient in need of such treatment.

The References

In rejecting claim 74 on prior art grounds, the examiner relies on the following reference:

Schwarzmann et al. (Schwarzmann), "Lysogangliosides: Synthesis and Use in Preparing Labeled Gangliosides," Methods in Enzymology, Vol. 138, pp. 319-341 (1987)

In rejecting claims 76 through 80 on non-prior art grounds, the examiner relies on the following reference:

Olney, "Excitotoxic Amino Acids and Neuropsychiatric Disorders," Annu. Rev. Pharmacol. Toxicol., Vol. 30, pp. 47-71 (1990)

The Issues

The issues presented for review are (1) whether the examiner erred in rejecting claim 74 under 35 U.S.C. § 103 as unpatentable over Schwarzmann; and (2) whether the

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examiner erred in rejecting claims 76 through 80 under 35 U.S.C. § 112, first paragraph, as based on a non-enabling disclosure.

Deliberations

Our deliberations in this matter have included evaluation and review of the following materials:

- (1) the instant specification, including Figures 1 through 7, and all of the claims on appeal;
- (2) applicants' Appeal Brief received October 15, 1996, the Reply Brief received April 27, 1997, the "Letter Supplemental to Reply Brief Submitting Exhibit A" dated May 6, 1997, the first Supplemental Reply Brief received August 11, 1997, and the second Supplemental Reply Brief received September 15, 1997;
- (3) the Examiner's Answer mailed February 25, 1997 (Paper No. 31); and
- (4) the above-cited prior art references.

On consideration of the record, including the above-listed materials, we reverse the examiner's rejection of claim 74 under 35 U.S.C. § 103. We affirm the rejection of claims 76 through 80 under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 103

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The Schwarzmans reference constitutes relevant prior art in view of its disclosure of a specific N-acyl-lysoganglioside, compound V. Schwarzmans illustrates the structural formula of compound V at page 325, and discloses its preparation at page 327.

We agree with the finding below that Schwarzmans compound V meets the terms of "active ingredient" recited in claim 74. That is, compound V is a species within the generic definition of N-acyl-lysoganglioside active ingredient recited in claim 74.

Nevertheless, Schwarzmans does not suggest the desirability of using compound V in combination with a pharmaceutically acceptable excipient. Schwarzmans does not provide adequate reason, suggestion, or motivation for using compound V in a pharmaceutical composition together with a pharmaceutically acceptable excipient.

On the contrary, we find that Schwarzmans does not disclose using compound V other than as an intermediate for preparing labeled gangliosides outside the scope of the present invention. Again, see the reaction scheme illustrated by Schwarzmans, page 325. For this reason, we conclude that Schwarzmans would not have led a person having ordinary skill in the art to the pharmaceutical composition recited in claim 74.

The examiner's decision, rejecting claim 74 under 35 U.S.C. § 103, is reversed.

35 U.S.C. § 112, First Paragraph

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The statutory basis for the enablement requirement is found in 35 U.S.C. § 112, first paragraph, which provides that:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without “undue experimentation.”

Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed. Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir. 1999).

Here, the examiner argues that claims 76 through 80 are based on a non-enabling disclosure. According to the examiner, any person skilled in the art would have faced undue experimentation in determining how to practice the full scope of applicants’ claimed invention. In setting forth this rejection, the examiner cites In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), where the court enumerated a number of factors which may be considered in determining whether a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary, (2) the amount of 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.

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All of the factors need not be reviewed when determining whether a disclosure is enabling. Rather, the Wands factors “are illustrative, not mandatory. What is relevant depends on the facts.” Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d at 1372, 52 USPQ2d at 1136.

The claimed invention is directed to a method of treating a variety of neurodegenerative disorders by administering a specified N-acyl-lysoganglioside, or derivatives or salts thereof, to a patient in need of such treatment. In the language of independent claim 76, applicants treat “disorders related to excitatory amino acid-induced neurotoxicity;” whereas claim 80 recites “A method of treating a patient suffering from the effect of neurotoxins.” These disorders include, inter alia, neurolathyrism, amyotrophic lateral sclerosis, epilepsy, hypoglycemia, CNS trauma, Huntington’s Disease, Alzheimer’s Disease, Parkinson’s Disease, Wernicke/Korsakoff Syndrome, and Jakob-Creutzfeldt Syndrome.

On reflection, we agree with the examiner that claims 76 through 80 cover a large area in view of the recitations “a method of treating disorders related to excitatory amino acid-induced neurotoxicity” and “a method of treating a patient suffering from the effect of neurotoxins.” The claims are broad in scope. This can be seen from Olney’s review article, indicative of the state of the prior art at the time applicants’ invention was made, outlining a large number of disorders “related to excitatory amino acid-induced neurotoxicity.” See particularly Olney, pages 52 through 61, section entitled

EXCITOTOXINS AND NEURODEGENERATIVE DISORDERS. As correctly found by the examiner, at the time applicants' invention was made, the prior art did not recognize effective means of treatment for a number of disorders discussed by Olney and embraced by the appealed claims, e.g., Huntington's Disease, Alzheimer's Disease, neuroleptism, Parkinson's Disease, Wernicke/Korsakoff Syndrome, Jakob-Creutzfeldt Syndrome, and amyotrophic lateral sclerosis. A number of these disorders have different etiologies, even though "related to" or "associated with" excitatory amino acid-induced neurotoxicity.

All in all, we believe that the examiner appropriately assessed the breadth of claims 76 through 80, and the state of the prior art, in determining that applicants' specification does not teach those skilled in the art how to use the full scope of the claimed invention without undue experimentation.

Further, as stated in In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970), "In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." Here, we agree with the examiner that applicants' claimed invention involves a relatively high degree of unpredictability. The claims at issue are drawn to a method of treating various neurodegenerative disorders by administering a specified pharmaceutically active ingredient to a patient in need of such treatment. The claimed invention involves unpredictable factors such as physiological activity, pharmacology, and therapeutic action of a specified N-acyl-lysoganglioside, or

derivatives or salts thereof. Also, the very nature of applicants' invention involves administering a pharmaceutically active ingredient to a human patient in need of treatment for "disorders related to excitatory amino acid-induced neurotoxicity" (claim 76) or "suffering from the effect of neurotoxins" (claim 80). Each method claim before us relates to a method of treating human patients.

Again, we believe that the examiner appropriately assessed the unpredictability of the art and the nature of the invention in determining that applicants' specification does not teach those skilled in the art how to use the full scope of the claimed invention without undue experimentation.

Applicants rely on in vitro and in vivo studies, described in their specification, as teaching any person skilled in the art how to practice the claimed invention. In response, the examiner argues that these studies are limited in scope because they involve only the NMDA receptor (Examiner's Answer, paragraph bridging pages 7 and 8). The examiner notes that there are at least three types of excitatory amino acid receptors capable of mediating excitotoxic events, i.e., NMDA, Quis, and KA (Olney, page 51, second paragraph). The most studied of these and reportedly the most abundant and widely distributed in the mammalian CNS, is the NMDA receptor. Several features distinguish the NMDA receptor from other subtypes of EAA receptor. (Id.) As stated in the concluding passage of the Olney publication,

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With the plethora of new information about the NMDA receptor-ionophore complex, one tends to forget that non-NMDA receptors can also mediate excitotoxic events. An instructive case in point is the recent evidence implicating KA receptors in domoate poisoning in which the resultant dementia is manifested most prominently in the elderly. Thus, although we know less about the physiology and makeup of non-NMDA receptors, as new information becomes available, it will probably lead to the recognition of new links between both NMDA and non-NMDA receptor-mediated processes and neuropsychiatric disorders. It is wise, therefore, to keep an open mind regarding the ultimate significance that can be ascribed to excitotoxic processes in human neuropsychiatric diseases, and the promise of anti-excitotoxic strategies for preventing such diseases. [Olney, page 66]

We agree that the in vitro and in vivo studies set forth in applicants' specification are limited in scope and insufficient to teach those skilled in the art how to use the full scope of the claimed invention without undue experimentation.

In the Appeal Brief received October 15, 1996, page 20, second complete paragraph, applicants state that

The Examiner's attention is . . . directed to the copy of the Declaration enclosed with the Proposed Amendment of May 4, 1994, which was submitted under 37 C.F.R. § 1.132 together with Attachments 1 and 2 and Enclosures 1 and 2 of said Declaration.

It can be seen that applicants invite attention to declaration evidence submitted in parent application 07/443,657 without presenting any argument or arguments, with a reasonable degree of specificity, based on that declaration. In this regard, applicants do not comply with the pertinent regulations governing practice and procedure before the Board of Patent Appeals and Interferences. See 37 CFR § 1.192(a) (1996), requiring that appellant's brief "set forth the authorities and arguments on which appellant will rely to maintain the appeal."

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Where, as here, applicants signal their intention to rely on declaration evidence, but do not present any argument or arguments based on that declaration, we shall not consider the Rule 132 declaration further.

Applicants argue that the active ingredients recited in claims 76 through 80, N-acyl-lysogangliosides, are derived from gangliosides which “play an important role in the nervous system” and “are useful in therapy for pathologies affecting the peripheral nervous system and in pathologies affecting the central nervous system.” On this point, applicants invite attention to the instant specification, paragraph bridging pages 13 and 14, including a list of reference citations therein. Applicants’ position appears to be that: (1) persons skilled in the art, at the time the invention was made, recognized that the parent gangliosides are useful in therapy for pathologies affecting the nervous system; and (2) it would not, therefore, require undue experimentation to practice the full scope of the claimed invention using N-acyl-lysogangliosides in view of the knowledge and information imparted by the specification. We disagree.

First, as we have discussed previously, at the time applicants’ invention was made the prior art did not recognize effective means of treatment for a number of neurodegenerative disorders embraced by the appealed claims. A number of these disorders have different etiologies, even though “related to” or “associated with” excitatory amino acid-induced neurotoxicity. See the Olney reference, particularly pages 52 through 61, section entitled EXCITOTOXINS AND NEURODEGENERATIVE DISORDERS.

Second, as best we can ascertain from the briefings, applicants do not point to any specific passage or passages in the literature citations listed in the specification, paragraph bridging pages 13 and 14. Nor does it appear that applicants have even supplied copies of these references for the record. Viewing the situation in this light, we find that applicants' argument predicated on pages 13 and 14 of the specification is incomplete. Third, according to applicants, an advantage of the products of the present invention (N-acyl-lysogangliosides), which "sets them apart" from gangliosides, is their ability to prevent and to combat neurotoxic action (specification, paragraph bridging pages 15 and 16).

In their Appeal Brief and Reply Brief, applicants refer to several literature articles published after the effective filing date of this application.¹ It is not entirely clear, however, why applicants rely on these post-dated articles. To the extent that applicants rely on these articles to "supplement" their specification, or to "substantiate" procedures outlined in the specification (Appeal Brief, sentence bridging pages 18 and 19; and page 22, last paragraph), such reliance is misplaced. See In re Glass, 492 F.2d 1228, 1232, 181 USPQ 31, 34 (CCPA 1974); Ex parte Hitzeman, 9 USPQ2d 1821, 1823-24 (Bd. Pat. App. & Interf. 1987). To the extent that applicants rely on these

¹ This application is a continuation of parent application 07/443,657, filed November 30, 1989. Further, according to the examiner, applicants "have an Italian foreign priority date of 12-02-88," based on Italian application 48618A/88 (Examiner's Answer, page 6, first paragraph).

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articles to “reaffirm” the adequacy of the disclosure of the present application (Appeal Brief, page 23, first paragraph), we have carefully reviewed applicants’ specification in conjunction with the cited articles. In our judgment, however, applicants have not established on this record that the specification teaches those skilled in the art how to use the full scope of the claimed invention without undue experimentation. As stated in In re Fisher, 427 F.2d at 839, 166 USPQ at 24, the first paragraph of 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. That is not the case here. We conclude that claims 76 through 80 are not sufficiently enabled by the specification as of the date that the patent application was first filed.

Other Issue

One further matter warrants attention.

The examiner finally rejected claim 74 under the judicially created doctrine of obviousness-type double patenting over claims 15 and 16 of U.S. Patent No. 5,350,841 (Office Action mailed December 13, 1995, Paper No. 25). In the “Response to Final Office Action” received June 27, 1996, applicants proffered a Terminal Disclaimer in an effort to overcome this rejection.

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The examiner stated that the double patenting rejection would be withdrawn “so long as the Terminal Disclaimer is found to be complete” (Advisory Action mailed August 12, 1996, Paper No. 29). Apparently, that is the case because the examiner does not repeat or refer to the rejection of claim 74 under the judicially created doctrine of obviousness-type double patenting in the Examiner’s Answer. Nevertheless, based on our review of the record, it does not appear that the Terminal Disclaimer has been processed by the PTO. On return of this application to the Examining Group, we recommend that the examiner review the Terminal Disclaimer dated June 27, 1996, and take steps to ensure that it is processed in the file.

Conclusion

In conclusion, for the reasons set forth in the body of this opinion, we reverse the examiner’s decision rejecting claim 74 under 35 U.S.C. § 103. We affirm the examiner’s decision rejecting claims 76 through 80 under 35 U.S.C. § 112, first paragraph. On return of this application to the Examining Group, we recommend that the examiner review the Terminal Disclaimer dated June 27, 1996, and take steps to ensure that it is processed in the file. Accordingly, the examiner’s decision is affirmed-in-part.

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

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AFFIRMED-IN-PART

Sherman D. Winters
Administrative Patent Judge

William F. Smith
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

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Birch, Stewart, Kolasch & Birch
P.O. box 747
Falls Church, VA 22040-0747