

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RHETT M. SCHIFFMAN

APPELLANT

Appeal 2008-4607
Application 10/379,157
Application Publication 2004/0175399
Technology Center 1600

Decided: September 18, 2008

Before SALLY GARDNER LANE, MICHAEL P. TIERNEY, and JAMES
T. MOORE *Administrative Patent Judges*.

LANE, *Administrative Patent Judge*.

DECISION ON APPEAL

I. STATEMENT OF THE CASE

The appeal is from a Final Rejection of claims 10 and 17-23. Claims 1-9, 11-16, and 24-33 are also pending in the application, but have been withdrawn. (App. Br. 5). 35 U.S.C. § 134. We have jurisdiction under 35 U.S.C. § 6(b). We reverse and enter a new ground of rejection.

The application was filed March 3, 2003. It was published on September 9, 2004, as Application Publication 2004/0175399 (“Pub. 2004/0175399”). The real party in interest is said to be Allergan, Inc. (App. Br. 3).

The Examiner rejected claims 10 and 17-23 under 35 U.S.C. § 102(e) over U.S. Patent No. 6,831,059 (“Donovan”), which was filed March 15, 2001, and issued December 14, 2004. The Examiner also relied on the following references as evidence of anticipation:

- Bramley et al., “Human Placental Gonadotrophin-Releasing Hormone (GNRH) Binding Sites: III. Changes in GnRH Binding Levels with Stage of Gestation,” *Placenta*, vol. 15, 733 (1994).
- Dgani¹ et al., “Clinical-pathological study of uterine leiomyomas with high mitotic activity,” *Acta Obstet. Gynecol. Scand.*, vol. 77, pp. 74-77 (1998).
- Eidne et al., “Gonadotropin-Releasing Hormone (GnRH)-Binding Sites in Human Breast Cancer Cell Lines and

¹ The Examiner and Appellant refer to this reference as “Dqani,” but the name of the first author is Dgani.

Inhibitory Effects of GnRH Antagonists,” *J. Clin. Endocrinol. Metab.*, vol. 64, pp. 425-32 (1987).

- Sion-Vardi et al., “Gonadotropin-Releasing Hormone Specific Biding Sites in Normal and Malignant Renal Tissue,” *J. Urol.*, vol. 148, pp. 1568-70 (1992).
- Vilos, “Uterine fibroids :relationships to reproduction,” *Minerva Ginecologica*, vol. 55, pp. 417-423 (2003).
- Volpe et al., “Pregnancy following regression of uterine submucosal leiomyoma with GnRH therapy; a case report,” *Eur. J. Obstet. & Gynecol.*, vol. 39, pp. 223-25 (1991).
- Wiznitzer, “Gonadotropin-Releasing Hormone Specific Binding Sites in Uterine Leiomyomata,” *Biochem. Biophys. Res. Comm.*, vol. 152, pp. 1326-31 (1988).

Appellant appeals the rejection of claims 10 and 17-23 under 35 U.S.C. § 102(e) over Donovan. Appellant argue separately for the patentability of claims 21-23. (App. Br. 15-16).

II. FINDINGS OF FACT

The record supports the following findings of fact as well as any other findings of fact set forth in this opinion, by at least a preponderance of the evidence.

1. Appellant’s claim 10 recites:

A method for treating a uterine fibroid, the method comprising the step of local administration of between about 10^{-3} U/kg² and

² Although Appellant’s Claims Appendix recited this term to be “ 10^{-3} U/kg,” we understand it to be “ 10^{-3} U/kg.”

about 2000 U/kg of a botulinum toxin to a uterine fibroid,
thereby treating a uterine fibroid.

(App. Br., Claims Appx. 18).

2. Appellant's specification provides that "[t]he botulinum toxin is selected from the group consisting of botulinum toxins types A, B, C, D, E, F and G" (Pub. 2004/0175399 ¶ [0100]; *see also* Pub. 2004/0175399 ¶¶ [0105], [0110], [0131], [0133]; [0143], and [0144]).

3. Appellant's specification acknowledges that "it has been disclosed that targeted botulinum toxins (i.e. with a non-native binding moiety) can be used to treat various conditions (see e.g. U.S. Pat. No 5,989,545, as well as WO 96/33273; WO 99/17806; WO 98/07864; WO 00/57897; WO 01/21213; WO 00/10598)." (Pub. 2004/0175399 ¶ [0042]).

4. Appellant's specification does not limit "a botulinum toxin" as excluding a "non-native binding moiety."

5. Donovan teaches that "[t]hose skilled in this art will also appreciate that an agent of this invention may also be administered to treat medical conditions which will benefit from a decrease of gonadotrophin levels in the body." (Donovan col. 17, ll. 41-44).

6. Donovan teaches:

GnRH antagonists and agonists have proven effective in the treatment of certain conditions which require a reduction of gonadotrophin release. For example, they have proven effective in the treatment of endometriosis, uterine fibroids, polycystic ovarian disease, precocious puberty and several gonadal steroid-dependent neoplasia, most notably cancers of the prostate, breast and ovary.

(Donovan col. 1, ll. 56-62).

7. Donovan teaches treating patients with “an agent [that] comprises a light chain component, a translocation component, and a targeting component.” (Donovan col. 12, ll. 30-32; *see also* Donovan Examples 1-5, col. 20, l. 45, through col. 22, l. 32).

8. The light chain taught in Donovan “may include a light chain of a botulinum toxin, a butyricum toxin, a tetani toxin or biologically active variants of these toxins.” (Donoavn col. 12, ll. 34-36).

9. The translocation component taught in Donovan comprises a heavy chain or modified heavy chain of *botulinum* toxin. (Donovan col. 12, ll. 60-66).

10. The “targeting component of [Donovan] is able to bind to a specific target cell receptor, for example, a GnRH receptor, preferably the pituitary GnRH receptor.” (Donovan col. 14, ll. 8-11).

11. Donovan teaches that “[f]or agents employing a natural, mutated or recombinant *botulinum* toxin A comprising the therapeutic, translocation and targeting component, an effective dose of an agent to be administered may be about 1 U to about 500 U of the *botulinum* toxin.” (Donovan col. 17, ll. 51-55).

12. Donovan teaches “‘Local administration’ means direct administration of a pharmaceutical at or to the vicinity of a site on or within an animal body, at which site a biological effect of the pharmaceutical is desired. Local administration excludes systemic routes of administration, such as intravenous or oral administration.” (Donovan col. 10, ll. 1-6).

13. Donovan teaches that

The routes of administration of the present invention include, but are not limited to, direct injection into the central nervous

system. . . . Other routes of administration include, without limitation, transdermal, peritoneal, subcutaneous, intramuscular, intravenous and intrarectal.

(Donovan col, 18, ll. 3-19)

14. Donovan does not expressly teach local administration of an agent into a uterine fibroid.

15. Donovan asserts that the botulinum toxin agent (called “LH_N-GnRH”) is effective in the treatment of endometriosis, prostate cancer, precocious puberty, endometrial cancer, and breast cancer, when administered locally to the pituitary gland. (*See* Donovan col. 20, l. 43, through col. 22, l. 31).

16. Wznitzer teaches “Gonadotropin-releasing hormone (GnRH) analogs can cause regression of uterine leiomyomata [fibroids] These results indicate, for the first time, the presence of specific binding sites for GnRH in uterine leiomyomata, suggesting a direct effect of GnRH analogs on this tissue.” (Wznitzer abstract).

17. Wznitzer does not use an agent that includes any part of the botulinum toxin.

18. Appellant’s claim 21 recites:

The method of claim 10, wherein treating the uterine fibroid further reduces the distortion of the endometrial cavity.

(App. Br., Claims Appx. 18).

19. Vilos states that “[f]rom the available evidence it can be concluded that removal of fibroids that distort the uterine cavity may be indicated in infertile women” (Vilos 419, first col., second paragraph).

20. Appellant’s claim 22 recites:

The method of claim 10, wherein treating the uterine fibroid further reduces the frequency of miscarriages.

(App. Br., Claims Appx. 18).

21. Volpe states: “In a patient harboring...leiomyomas, adversely affecting conception and pregnancy outcome, GnRHa [gonadotropin/releasing hormone analog] treatment may be an initial approach” (Volpe abstract).

22. Volpe does not use an agent that includes any part of the botulinum toxin.

23. Appellant’s claim 23 recites:

The method of claim 10, wherein treating the uterine fibroid further prevents the fibroid from becoming malignant.

(App. Br., Claims Appx. 18).

24. Dgani states: “The benign clinical behavior of such tumors supports their current designation as mitotically active leiomyomas, thus deleting the previous misnomer ‘smooth muscle tumors of uncertain malignant potential.’” (Dgani abstract).

III. LEGAL PRINCIPLES

Claimed subject matter is anticipated by the teachings of a reference only if the claimed subject matter is identically disclosed or described by the teachings of the reference. *Richardson v. Suzuki Motor Co., Ltd.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989) (citation omitted) (“The identical invention must be shown in as complete detail as is contained in the patent claim.”). To be anticipated, the claimed subject matter must be disclosed “clearly and

unequivocally” in the reference. *In re Arkley*, 455 F.2d 586, 587 (C.C.P.A 1972) (“Thus, for the instant [anticipation] rejection... to have been proper, the ...reference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference.”).

On the other hand, “[w]hen a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.” *KSR Int’l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1740 (2007). “Common sense teaches . . . that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle.” *Id.* at 1742.

IV. ANALYSIS

Appellant’s claim 10 recites:

A method for treating a uterine fibroid, the method comprising the step of local administration of between about 10^{-3} U/kg and about 2000 U/kg of a botulinum toxin to a uterine fibroid, thereby treating a uterine fibroid.

(FF³ 1). While Appellant’s specification provides that “[t]he botulinum toxin is selected from the group consisting of botulinum toxins types A, B, C, D, E, F and G . . . ” (FF 2), it also acknowledges that “it has been disclosed that targeted botulinum toxins (i.e. with a non-native binding

³ Finding of Fact.

moiety) can be used to treat various conditions” (FF 3). Appellant’s specification does not limit “a botulinum toxin” to excluding “non-native binding moieties.” (FF 4). “During examination, ‘claims ... are to be given their broadest reasonable interpretation consistent with the specification, and . . . claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art.’” *In re American Academy of Sci. Tech Center*, 367 F.3d 1359, 1364 (Fed. Cir. 2004) (citation omitted). Thus, the claim term “a botulinum toxin” includes botulinum toxins of types A, B, C, D, E, F, and G, either alone or with an attached “non-native binding moiety.”

Donovan teaches that “[t]hose skilled in this art will . . . appreciate that an agent of this invention may also be administered to treat medical conditions which will benefit from a decrease of gonadotrophin levels in the body.” (FF 5). In regard to the conditions that would benefit from a decrease in gonadotrophin levels, Donovan teaches that GnRH antagonists and agonists “have proven effective in the treatment of endometriosis, uterine fibroids, polycystic ovarian disease, precocious puberty and several gonadal steroid-dependent neoplasia, most notably cancers of the prostate, breast and ovary.” (FF 6).

Donovan teaches treating patients with “an agent [that] comprises a light chain component, a translocation component, and a targeting component.” (FF 7). The light chain and translocation components can be the light chain and heavy chain, respectively, of botulinum toxin (FFs 8 and 9), while the targeting component can bind to a GnRH receptor (FF 10).

Donovan teaches that “an effective dose of an agent to be administered may be about 1 U to about 500 U of the *botulinum* toxin” (FF

11), which overlaps with the claimed range of “between about 10^{-3} U/kg and about 2000 U/kg” (FF 1). Donovan teaches “local administration” of the agent, wherein “[l]ocal administration’ means direct administration of a pharmaceutical at or to the vicinity of a site on or within an animal body, at which site a biological effect of the pharmaceutical is desired. Local administration excludes systemic routes of administration, such as intravenous or oral administration.” (FF 12). Donovan does not expressly teach administration of an agent into a uterine fibroid. (FF 14). The Examiner has not pointed us to any teaching in Donovan that “‘clearly and unequivocally’ directs those skilled in the art to make this selection nor any indication that [the prior art] ever made the selection [itself].” *Arkley*, 455 F.2d at 588. Thus, we conclude that Donovan does not clearly and unequivocally disclose the claimed method of treating a uterine fibroid with a botulinum toxin without any need for picking, choosing, and combining various disclosures. Accordingly, we reverse the rejection under 35 U.S.C. § 102(e) over Donovan.

On the other hand, while Donovan acknowledges that GnRH antagonists and agonists are effective in treating uterine fibroids (FF6), Wiznitzer teaches that the GnRH analogs known at the time may act directly on the fibroid (FF 16). Thus, those of skill in the art would have had reason to combine their teachings to administer the botulinum toxin agents of Donovan, which Donovan asserts are effective when administered to the pituitary gland (FF 15), directly to uterine fibroid tissue. There would have been a reasonable expectation of success in this method because Donovan teaches local administration of botulinum toxin agents. (FFs 12 and 13). Those of skill in the art would have been able to “implement a predictable

variation,” *KSR, supra*, of the methods expressly taught in Donovan, in light of the teaching of Wznitzer, and Appellant’s claimed methods would have been obvious. Accordingly, we enter a new ground of rejection for claims 10 and 17-23 under 35 U.S.C. § 103(a) over Donovan and Wznitzer.

Turning to the arguments that apply to our new grounds of rejection under 35 U.S.C. § 103(a), Appellant first argued that

[a] person of ordinary skill in the art would not consider botulinum toxin to be a GnRH agonist or antagonist. As the Donovan specification explains, GnRH antagonists are existing drugs that act to decrease gonadotrophin secretion by binding competitively to the GnRH receptors. (Donovan at column 1, lines 45-46, 53-55) Although recombinant and chemically modified botulinum toxin is used to create the therapeutic agent claimed in Donovan, the botulinum toxin does not bind to the GnRH receptor. (*Id.* at columns 12 through 14) The targeting component of the agent, not the botulinum toxin, is the moiety which binds the receptor. (*Id.* at column 14, lines 8-12)[.]

(App. Br. 13; *see also* Reply Br. 5). Appellant’s specification acknowledges that native botulinum toxin can be modified with non-native binding moieties (FF 3), and neither Appellant’s specification nor claim 10 limits the claim term “a botulinum toxin” to exclude these moieties (*see* FFs 1 and 4). *See American Academy, supra*.

In regard to claims 21-23, Appellant argued that the claimed subject matter, methods to reduce distortion of the endometrial cavity, frequency of miscarriages, and the prevention of a fibroid from becoming malignant, respectively, is not disclosed in Donovan. (App. Br. 15). Appellant asserted, further, that

"When the claimed composition or machine is disclosed identically by the reference, an additional reference may be

relied on to show that the primary reference has an 'enabled disclosure.'" *In re Donohue*, 766 F.2d 531, 226 USPQ 619, 621 (Fed. Cir. 1985). In the instant case, the claimed subject matter disclosed in claims 21-23 is not identically disclosed by Donovan and therefore, the cited extrinsic evidence [Vilos, Volpe, and Dgani] cannot be relied on to show that the primary reference anticipates the claimed subject matter.

(App. Br. 15-16). The Examiner did not cite Vilos, Volpe, and Dgani to show that Donovan is enabled, but instead to show that those of skill in the art would have known that the claimed effects are “effects *generally* achieved by any treatment of uterine fibroids that inhibits their growth and further development and/or causes their regression.” (Ans. 17). These references serve the same function under our new grounds of rejection.

Vilos states that “removal of fibroids that distort the uterine cavity may be indicated in infertile women” (FF 19), thus providing evidence that those in the art knew that treatment of a fibroid would “[reduce] the distortion of the endometrial cavity” (FF 18), as claimed. Appellant argued that “Vilos does not qualify as a prior art reference under 35 U.S.C. § 102 because it was not published until October 2003, seven months after the earliest priority date of the present application.” (App. Br. 15). References that are not technically prior art are still properly cited to establish the level of ordinary skill in an art at and around the time of the present invention. *See In re Erlich*, 22 U.S.P.Q.2d 1463, 1465 (BPAI 1992). Appellant has not provided us with any evidence to convince us that those in the art first learned that fibroids distort the endometrial cavity less than seven months before Vilos was published. Thus, those of skill in the art would have used the agents taught in Donovan to treating fibroids and thus reduce the

distortion of the endometrial cavity they cause, after combining the teachings of Donovan and Wiznitzer.

Volpe discloses that gonadotropin/releasing hormone analog treatment is an initial approach to treating uterine fibroids that adversely affect conception and pregnancy outcome, that is miscarriages (FF 21), demonstrating that those of skill in the art would have used the botulinum toxin agent in Donovan, which is a GnRH analog because it binds to a gonadotrophin receptor (FF 10), to “[reduce] the frequency of miscarriages.” (FF 20), after combining the teachings of Donovan and Wiznitzer.

Finally, Dgani states: “The benign clinical behavior of such tumors supports their current designation as mitotically active leiomyomas, thus deleting the previous misnomer ‘smooth muscle tumors of uncertain malignant potential.’” (FF 24). Thus, after combining the teachings of Donovan and Wiznitzer, those of skill in the art would have used the botulinum toxin of Donovan to prevent a uterine fibroid from “becoming malignant,” as claimed (FF 23), as part of the overall treatment of the uterine fibroid.

Accordingly, claims 21-23 are not separately patentable under the new grounds of rejection under 35 U.S.C. § 103(a) over Donovan and Wiznitzer.

V. ORDER

Upon consideration of the record and for the reasons given, the Examiner’s rejection of claims 10 and 17-23 under 35 U.S.C. § 102(e) over Donovan, as evidenced by Vilos, Volpe, Dgani, and/or Wiznitzer is REVERSED;

We enter a new grounds of rejection for claims 10 and 17-23 under 35 U.S.C. § 103(a) over Donovan and Wiznitzer for the reasons set forth herein. 37 C.F.R. § 41.50(b).

37 C.F.R. § 41.50(b) provides that, “[a] new grounds of rejection pursuant to this paragraph shall not be considered final for judicial review.”

37 C.F.R. § 41.50(b) also provides that the Appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new grounds of rejection to avoid termination of proceedings as to the rejected claims:

(1) Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner; or

(2) Request that the proceeding be reheard under 37 C.F.R. § 41.52 by the Board upon the same record.

REVERSED; NEW GROUNDS ENTERED 37 C.F.R. § 41.50(b)

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