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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte EDWARD M. GILLIS, BARBARA J.F. LAIDLAW, JOHN CULWELL, JAMES A. FILICE, PETER WICKMAN, ANDREW I. POUTIATINE, and JOHN S. DINKA

Appeal 2010-009318
Application 10/922,239
Technology Center 1600

Before DONALD E. ADAMS, FRANCISCO C. PRATS, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims to methods of inducing systemic analgesia. The Examiner entered a rejection for obviousness.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm. As to one group of claims, however, we designate our affirmance a new ground under 37 C.F.R. § 41.50(b).

STATEMENT OF THE CASE

Claims 28-67 stand rejected and appealed (App. Br. 3). Claims 28, 32, and 63 are representative and reads as follows:

> 28. A method of inducing systemic analgesia in a subject, the method comprising systemically administering sufentanil to the subject at a therapeutically effective rate to provide substantially continuous delivery of sufentanil at about 10 µg/hr over a period of at least 24 hours, wherein said administering induces systemic analgesia in the subject, and wherein said sufentanil is formulated in a sufentanil formulation comprising an amount of sufentanil sufficient for substantially continuous delivery of sufentanil at about 10 µg/hr over said period of at least 24 hours.
>
> 32. The method of claim 28, wherein said period is at least 30 days.
>
> 63. The method of claim 28, wherein the sufentanil is not delivered using a mechanical or electro-mechanical infusion pump.

The sole rejection before us for review is the Examiner's rejection of claims 28-67 under 35 U.S.C. § 103(a) as obvious over Wagemans[1] and Wappler[2] (Ans. 3-5).

[1] Michel F.M. Wagemans et al., *Long-Term Spinal Opioid Therapy in Terminally Ill Cancer Pain Patients*, 2 THE ONCOLOGIST 70-75 (1997).

[2] F. Wappler et al., *Analgesia and sedation with sufentanil in intensive care medicine*, 33 ANÄSTHESIOL. INTENSIVMED. NOTFALLMED. SCHMEUTHER. 18-26 (1998) (as translated). The Examiner originally relied only on a PubMed abstract of Wappler entered into the electronic file on July 18, 2007. Appellants provided the full text of the Wappler article in German, along with an English translation of the article with their response entered June 4, 2008 (*see* App. Br. Evidence Appendix, Exhibit 2).

OBVIOUSNESS

The Examiner found that Wagemans taught long term opioid therapy by systemically administering the minimally effective dose of sufentanil as the preferred analgesic (Ans. 3). The Examiner noted that Wagemans taught administering the analgesic "by implanted infusion pump for months or years and provid[ing] constant infusion" (*id.* at 3-4) (citing Wagemans 73).

The Examiner found, however, that Wagemans differed from the rejected claims in that Wagemans did not "explicitly teach the dose of sufentanil as instantly claimed" (*id.* at 4). To meet that deficiency, the Examiner cited Wappler as teaching continuous infusion of sufentanil to intensive care patients for sedation and analgesia at dosage rates encompassed by the claims, "assuming the patient has average body weight of 60 kg" (*id.*).

Based on the references' teachings the Examiner concluded that an ordinary artisan would have considered it obvious "to treat pain using continuous sufentanil infusion at [a] minimal effective dose as taught by Wagemans" using the dosage rates disclosed by Wappler "because Wappler et al. teaches that such a dose when provided as continuous infusion, is suitable for intensive care patients for sedation and analgesia without significant respiratory depression during spontaneous breathing" (*id.*). The Examiner further reasoned that an ordinary artisan would have "readily optimized effective dosages and concurrent administration regimens as determined by good medical practice and the clinical condition of the individual patient" (*id.* at 12-13). In particular, the Examiner found that determining a suitable dosage "for treating pain involving sufentanil and its administration period would have been routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information disclosed by Wappler" (*id.* at 13).

Appellants contend that, because Wappler teaches adjusting the sufentanil administration rate depending on the patient's sedation state, "Wappler teaches away from substantially continuous delivery at the claimed rates over a period of at least 24 hours" (App. Br. 9). Thus, Appellants urge, "[b]y combining Wappler with Wagemans to arrive at the claimed invention, the Office disregards Wappler's teaching to adjust the amount of drug per unit time based on individual patient need rather than maintain substantially continuous delivery at a specified rate for at least a 24 hr period" (*id.*; *see also* Reply Br. 2-3).

Appellants also contend that Wagemans teaches away from the claimed invention because, rather than teaching systemic administration as the rejected claims require, Wagemans instead specifically discusses advantages of local administration when compared to systemic administration (App. Br. 10; *see also* Reply Br. 4-5). Moreover, Appellants argue, an ordinary artisan would not have had an apparent reason to combine the two references' teachings (App. Br. 11).

Specifically, Appellants contrast Wagemans' local administration of sufentanil to the spine (*id.*), with Wappler's intravenous administration by syringe pump (*id.* at 12-13), and reason that an ordinary artisan would not have applied a Wappler's intravenous sufentanil dosage "in the context of local spinal administration because in local spinal administration the sufentanil is delivered directly to the receptors it will act upon" (*id.* at 13). Accordingly, Appellants conclude, "one of ordinary skill in the art would have no apparent reason to apply the dosage regime for systemic administration of Wappler in the context of the local spinal administration described by Wagemans" (*id.*; *see also* Reply Br. 6-7).

We select claim 28 as representative of the rejected claims. *See* 37 C.F.R. § 41.37(c)(1)(vii).

Appellants' arguments do not persuade us that the Examiner erred in concluding that an ordinary artisan viewing Wagemans and Wappler would have considered claim 28 prima facie obvious.

Claim 28 recites a method of inducing systemic analgesia in a subject. Claim 28 requires the practitioner to induce systemic analgesia in the subject by systemically administering sufentanil at a therapeutically effective rate to provide substantially continuous delivery of sufentanil at about 10 µg/hr over a period of at least 24 hours. The claim also requires the sufentanil to be in a formulation that contains sufficient sufentanil for substantially continuous delivery of sufentanil at about 10 µg/hr over the period of at least 24 hours.

Wagemans teaches that, in "terminally ill cancer patients with refractory pain, long-term spinal opioid therapy may provide a profound analgesia with minimal side effects" (Wagemans 70). Wagemans notes in particular that, "[f]or epidural administration, it is preferable to use lipid soluble opioids (sufentanil)" (*id.*).

Wagemans notes that "[e]pidural opioid administration reaches the receptor in two ways: *systemic absorption* and penetration of dura mater and arachnoid. Plasma opioid concentrations after epidural administration are similar to plasma opioid concentrations after intramuscular injections when using lipophilic agents such as sufentanil" (*id.* at 72 (emphasis added)).

Wagemans teaches that its opioid infusion can be accomplished using a "totally implanted catheter and infusion pump [which] is reserved for patients with a life expectancy of months or years. Its reservoir is refilled percutaneously every 14 to 21 days and provides a constant infusion rate" (*id.* at 73).

Given these teachings, we agree with the Examiner that an ordinary artisan would have been prompted by Wagemans to epidurally administer sufentanil at a

constant rate using an implanted infusion pump, thereby achieving the substantially continuous delivery of the drug as required by claim 28, as well as the systemic delivery and analgesia required by the claim.

While the Examiner points us to no specific empirical dosage teachings in Wagemans, Wappler discloses a broad range of sufentanil dosages that provide analgesic relief in intensive care patients (Wappler 5, 8-9),[3] which Appellants do not dispute as encompassing the claimed dosage rate. We therefore find that the Examiner has provided adequate evidentiary support for reasoning that the sufentanil dosage rate was a result effective parameter that an ordinary artisan would have optimized (*see* Ans. 12-13), and that an ordinary artisan would therefore have optimized the dosage in Wagemans' continuous infusion treatment method.

It is well settled that "the discovery of an optimum value of a variable in a known process is usually obvious." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1368 (Fed. Cir. 2007). The rationale for determining the optimal parameters for prior art result effective variables "flows from the 'normal desire of scientists or artisans to improve upon what is already generally known.'" *Id.* (quoting *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003)).

In general, however, "an applicant may overcome a *prima facie* case of obviousness by establishing 'that the [claimed] range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range.'" *In re Peterson*, 315 F.3d at 1330 (quoting *In re Geisler*, 116 F.3d 1465, 1469-70 (Fed. Cir. 1997).

[3] The translation of Wappler supplied by Appellants in the Evidence Appendix of the Appeal Brief does not have page numbers; we therefore refer to the page numbers as if the first page was page 1, and the remaining pages were consecutively numbered.

Thus, it may be true that Wappler administers sufentanil intravenously, as Appellants argue, rather than epidurally. However, given the broad range of useful dosages described in Wappler, we are not persuaded that the Examiner has failed to provide an adequate evidentiary basis for concluding that an ordinary artisan practicing Wagemans' continuous delivery method would have optimized the sufentanil dosage. As Appellants point us to no evidence that the dosage recited in claim 28 provides an unexpected result, and is therefore critical, *see Peterson,* 315 F.3d at 1330, we are not persuaded that the claimed dosage would have been unobvious over the cited references, despite the fact that the two cited references do not appear to describe the same route of drug administration.

We are also not persuaded that the references teach away from practicing the process recited in claim 28. It may be true that Wappler discloses treating the patients in its study by adjusting the sufentanil dosage rate to maintain a particular level of sedation (Wappler 3). However, Appellants point to nothing in Wappler that disparages the continuous dosage administration indicated for the patients described in Wagemans treatment protocol (Wagemans 73).

We are also unconvinced that Wagemans teaches away from the systemic administration required by claim 28.

During examination, the PTO must interpret terms in a claim using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

We note that claim 28 requires "systemically administering sufentanil" (App. Br. 18). However, Appellants' Specification explicitly states that "[t]he term

'systemic delivery' *is meant to encompass all parenteral routes of delivery which permit drug to enter into the systemic circulation*, e.g., intravenous, intraarterial, intramuscular, subcutaneous, intra-adipose tissue, intra-lymphatic, etc." (Spec. 11 ¶ [0056] (emphasis added).)

As noted above, Wagemans explicitly states that its epidural administration results in systemic absorption of the analgesic, and notes that plasma concentrations of the drug are comparable to those achieved by intramuscular injection (Wagemans 72). Because the term "systemically delivering" in claim 28 encompasses any non-intestinal delivery route which results in drug entry into the systemic circulation, and because Wagemans explicitly discloses that its epidural administration achieves that result, we are not persuaded that claim 28 fails to encompass Wagemans delivery method.

Accordingly, as Appellants' arguments do not persuade us that the Examiner failed to make a prima facie case that an ordinary artisan would have considered claim 28 obvious in view of Wagemans and Wappler, we affirm the Examiner's rejection of that claim over those references. Claims 29-31, 35-38, 42-45, 49-52, and 56-59 fall with claim 28 as they were argued in the same claim grouping (*see* App. Br. 6).

Appellants separately argue that the process recited in claim 32, which recites substantially continuous delivery of sufentanil for at least 30 days (*see id.* at 18), was not taught or suggested by the references because "Wagemans teaches that its implanted infusion pump is refilled percutaneously every 14 to 21 days. This suggests that the formulation utilized in the implanted infusion pump of Wagemans does not **comprise an amount of sufentanil sufficient for the substantially continuous delivery of sufentanil over a period of at least 30 days**" (App. Br. 14 (citing Wagemans 73); *see also* Reply Br. 7-8).

The Examiner responds that "***Firstly:*** refilling of the device is not excluded by the claims. ***Secondly:*** refilling of the device indicating that the sufentanil is being given in continuous uninterrupted manner. ***Thirdly:*** Wagemans teaches delivery for months or years" (Ans. 15).

We find that the Examiner has the better position here. We note that claim 30 requires the process to use a sufentanil formulation comprising an amount of sufentanil sufficient for substantially continuous delivery of sufentanil at about 10 µg per hour over a period of at least 30 days (*see* App. Br. 18).

However, Wagemans describes using a "totally implanted catheter and infusion pump [which] is reserved for patients with a life expectancy of months or years. Its reservoir is refilled percutaneously every 14 to 21 days and provides a constant infusion rate" (Wagemans 73). Thus, given that Wagemans suggests at least one refill, Wagemans therefore also suggests not only substantially continuous administration of sufentanil for 42 days, but also preparation of an amount of sufentanil sufficient to achieve substantially constant infusion for that length of time.

Accordingly, as Appellants' arguments do not persuade us that the Examiner erred in concluding that an ordinary artisan would have considered claim 32 prima facie obvious in view of Wagemans and Wappler, we affirm the Examiner's rejection of that claim over those references. Claims 33, 34, 39-41, 46-48, 53-55, and 60-62 fall with claim 32 as they were argued in the same claim grouping (*see* App. Br. 6).

Appellants also argued claims 63-67 separately (*see id.*). Appellants urge that the Examiner failed to "demonstrate explicitly that the combined prior art references teach or suggest all the claimed limitations. Appellants respectfully submit that the Examiner has failed to provide such an explicit analysis with

respect to the instant claims" (*id.* at 15). Specifically, Appellants argue, "the Examiner has failed to demonstrate a teaching or suggestion in the prior art with respect to the negative limitation of claims 63-67" (*id.*).

While we agree with Appellants that the Examiner did not make explicit the requisite findings to support the prima facie case, we nonetheless conclude that claims 63-67 would have been prima facie obvious to an ordinary artisan viewing Wagemans and Wappler.

Claim 63 recites "[t]he method of claim 28, wherein the sufentanil is not delivered using a mechanical or electro-mechanical infusion pump." Claims 64-67 recite similar methods, except that they depend from independent claims 35, 42, 49, and 56, respectively, which in turn recite essentially the same process as claim 28, except with higher sufentanil dosages (*see* App. Br. 18-20).

The Supreme Court has advised that "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, *there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR Int' l Co. v. Teleflex Inc*., 550 U.S. 398, 418 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added).

In this case, the Examiner's obviousness rationale regarding claims 63-67 states in its entirety that "applicants failed to show unexpected results obtained from using specific delivery devices, and the exclusion of infusion pumps does not impart patentability to the claims, absent evidence to the contrary" (Ans. 5).

Thus, we agree with Appellants that the Examiner failed to point to any specific teaching in either of the cited references explaining why an ordinary artisan would have considered it obvious to use a delivery device or method other than Wageman's infusion pump (Wagemans 73) to achieve substantially continuous delivery of sufentanil. We therefore also agree with Appellants that the

Examiner failed to articulate a fact-based rationale to support the obviousness conclusion.

We are not persuaded, however, that the Examiner erred in concluding that an ordinary artisan would have considered claims 63-67 obvious over Wagemans and Wappler. Specifically, as discussed above, Wagemans suggests substantially continuous delivery of sufentanil for extended periods in certain patients (Wagemans 73 ("A totally implanted catheter and infusion pump is reserved for patients with a life expectancy of months or years. Its reservoir is refilled percutaneously every 14 to 21 days and provides a constant infusion rate.")).

While it is true that Wagemans' continuous drug delivery uses a device explicitly excluded from claims 63-67, the Wappler study similarly describes prior studies that "recommend the continuous giving of the [analgesic] drugs via syringe pumps" (Wappler 1), which, as Appellants concede (App. Br. 12-13), would have suggested that continuous intravenous administration would be useful to achieve and sustain analgesia. Wappler also discloses another study which administered sufentanil in a "maintenance phase," again suggesting continuous administration of the drug (Wappler 9).

Given Wappler's suggestion that intravenous administration was a suitable technique for achieving continuous analgesic drug delivery, we conclude that an ordinary artisan would have considered it obvious to use means other than mechanical or electro-mechanical infusion pumps to continuously administer sufentanil for extended periods of time, including the extended periods described by Wageman. We therefore also conclude that claims 63-67 would have been obvious to an ordinary artisan, and accordingly affirm the Examiner's rejection of those claims over those references.

However, as our rationale differs from that advanced by the Examiner, we designate our affirmance of claims 63-67 a new ground of rejection under 37 C.F.R. § 41.50(b).

SUMMARY

We affirm the Examiner's rejection of claims 28-62 as obvious over Wagemans and Wappler.

We also affirm the Examiner's rejection of claims 63-67 over Wagemans and Wappler, but designate the affirmance as a new ground under 37 C.F.R. § 41.50(b).

TIME PERIOD

This decision contains a new ground of rejection pursuant to 37 C.F.R. § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 C.F.R. § 41.50(b) provides "[a] new ground 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 appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. 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 . . . .
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same record . . . .

AFFIRMED, 37 C.F.R. § 41.50(b)

cdc